

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
12 September 2002 (12.09.2002)

PCT

(10) International Publication Number
WO 02/069900 A2

(51) International Patent Classification⁷: **A61K**

(21) International Application Number: PCT/US02/06518

(22) International Filing Date: 1 March 2002 (01.03.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/272,751 1 March 2001 (01.03.2001) US

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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS FOR TREATING GENETICALLY-DEFINED PROLIFERATIVE DISORDERS WITH HSP90 INHIBITORS

Type of Aberration	Background Literature	Affected Gene(s)	Protein Domain	Fusion Protein	Disease
t(9; 22)(q34; q11)	de Klein, A. et al. Nature 300, 765-767 (1982)	<i>CABL</i> (9q34) <i>BCR</i> (22q11)	tyrosine kinase serine kinase	serine + tyrosine kinase	CML/ALL
inv14 (q11; q32)	Baer, R., Chen, K.-C., Smith, S. D. & Rabbitts, T. H. Cell 43, 705-713 (1985); Denny, C. T. et al. Nature 320, 549-551 (1986)	TCR- α (14q11) VH- (14q32)	TCR- α Ig VH	VH-TCR- α	T/B-cell lymphoma
t(1; 19)(q23; p13.3)	Kamps, M. P., Murre, C., Sun, X.-H. & Baltimore, D. Cell 60, 547-555 (1990); Nourse, J. et al. Cell 60, 535-545 (1990)	<i>PBX1</i> (1q23) <i>E2A</i> (19p13.3)	HD AD-b-HLH	AD + HD	pre-B-ALL
t(17; 19)(q22; p13)	Hunger, S. P., Ohyashiki, K., Toyama, K. & Clearly, M. L. Genes Dev. 6, 1608-1620 (1992); Inaba, T. et al. Science 257, 531-534 (1992)	<i>HLF</i> (17q22) <i>E2A</i> (19p13)	bZIP AD-b-HLH	AD + bZIP	pro-B-ALL
t(15; 17)(q21-q11-22)	Giliard, E. F. & Solomon, E. Sem. Cancer Biol. 4, 359-368 (1993)	<i>PML</i> (15Q21) <i>RARA</i> (17q21)	Zinc-finger Retinoic acid receptor- α	Zinc-finger + RAR DNA and ligand binding	APL
t(11; 17)(q23; q21.1)	Chen, Z. et al. EMBO J. 12, 1161-1167 (1993)	<i>PLZF</i> (11q23) <i>RARA</i> (17q21)	Zinc-finger Retinoic acid receptor α	Zn-finger + RAR DNA and ligand binding	APL
t(4; 11)(q21; q23)	Djabali, M. et al. Nature Genet. 2, 113-118 (1992); Gu, Y. et al. Cell 71, 701-708 (1992)	<i>MLL</i> (11q23) <i>AF4</i> (4q21)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + (Ser-pro)	ALL/pre-B-ALL/ ANLL
t(9; 11)(q21; q23)	Nakamura, T. et al. Proc. natn. Acad. Sci. U.S.A. 90, 4631-4635 (1993); Lida, S. et al. Oncogene 8, 3085-3092 (1993)	<i>MLL</i> (11q23) <i>AF9/MLLT3</i> (9p22)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + (Ser-Pro)	ALL/pre-B-ALL/ ANLL
t(11; 19)(q23; p13)	Tkachuk, D. C., Kohler, S. & Cleary, M. L. Cell 71, 691-700 (1992); Yamamoto, K. et al. Oncogene 8, 2617-2625 (1993)	<i>MLL</i> (11q23) <i>ENL</i> (19p13)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + Ser-Pro	pre-B-ALL/ T-ALL/ ANLL

(57) Abstract: The invention relates generally to methods of treating cell proliferative diseases with HSP90 inhibitors and, depending on the specific aspect and embodiment(s) claimed, to the treatment of proliferative diseases that are associated with fusion proteins, e.g., bcrabl, or mutant proteins or cellular protein isoforms, e.g., mutant forms of p53.



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Methods for Treating Genetically-Defined Proliferative Disorders with HSP90 Inhibitors

Field of the Invention

The field of the invention relates to chemotherapeutic treatments of proliferative disorders, including rheumatoid arthritis and neoplasias.

Background of the Invention

The following description includes information that may be useful in understanding the present invention. It is not an admission that any of the information provided herein is prior art, or relevant, to the presently claimed inventions, or that any publication specifically or implicitly referenced is prior art.

The eukaryotic heat shock protein 90s (HSP90s) are ubiquitous chaperone proteins that are involved in folding, activation and assembly of a wide range of proteins, including key proteins involved in signal transduction, cell cycle control and transcriptional regulation. HSP90 proteins are highly conserved in nature (see, e.g., NCBI accession # P07900 (SEQ ID NO: 318) and XM004515 (SEQ ID NOs: 319 and 320) (human α and β HSP90, respectively), P11499 (SEQ ID NO: 321) (mouse), AAB23369 (SEQ ID NO: 322) (rat), P46633 (SEQ ID NO: 323) (chinese hamster), JC1468 (SEQ ID NO: 324) (chicken), AAF69019 (SEQ ID NO: 325) (fleshfly), AAC21566 (SEQ ID NO: 326) (zebrafish), AAD30275 (SEQ ID NO: 327) (salmon), AAC48718 (SEQ ID NO: 328) (pig), NP 015084 (SEQ ID NO: 329) (yeast), and CAC29071 (SEQ ID NO: 330) (frog).

Researchers have reported that HSP90 chaperone proteins are associated with important signaling proteins, such as steroid hormone receptors and protein kinases, including many that are implicated in tumorigenesis, e.g., Raf-1, EGFR, v-Src family kinases, Cdk4, and ErbB-2 (Buchner J., 1999, *TIBS*, 24:136-141; Stepanova, L. *et al.*, 1996, *Genes Dev.* 10:1491-502; Dai, K. *et al.*, 1996, *J. Biol. Chem.* 271:22030-4). *In vivo* and *in vitro* studies indicate that certain co-chaperones, e.g., Hsp70, p60/Hop/Sti1, Hip, Bag1, HSP40/Hdj2/Hsj1, immunophilins, p23, and p50, may assist HSP90 in its function (Caplan, A., 1999, *Trends in Cell Biol.*, 9: 262-68).

Ansamycins are antibiotics derived from *Streptomyces hygroscopicus* which are known to inhibit HSP90s. These antibiotics, e.g., herbimycin A (HA) and geldanamycin (GM), as well as other HSP90 inhibitors such as radicicol, bind tightly to an N-terminal pocket in HSP90 (Stebbins, C. *et al.*, 1997, *Cell*, 89:239-250). This pocket is highly conserved and has weak

homology to the ATP-binding site of DNA gyrase (Stebbins, C. *et al.*, *supra*; Grenert, J.P. *et al.*, 1997, *J. Biol. Chem.*, 272:23843-50). ATP and ADP have been shown to bind this pocket with low affinity, and HSP90 itself has been shown to have weak ATPase activity (Proromou, C. *et al.*, 1997, *Cell*, 90: 65-75; Panaretou, B. *et al.*, 1998, *EMBO J.*, 17: 4829-36). *In vitro and in vivo* studies have demonstrated that occupancy of the N-terminal pocket of HSP90 by ansamycins and other inhibitors alters HSP90 function and inhibits client protein folding. At high concentrations, ansamycins and other HSP90 inhibitors have been shown to prevent binding of client protein substrates to HSP90 (Scheibel, T., H. *et al.*, 1999, *Proc. Natl. Acad. Sci. U S A* 96:1297-302; Schulte, T. W. *et al.*, 1995, *J. Biol. Chem.* 270:24585-8; Whitesell, L., *et al.*, 1994, *Proc. Natl. Acad. Sci. U S A* 91:8324-8328). Ansamycins have also been demonstrated to inhibit the ATP-dependent release of chaperone-associated protein substrates (Schneider, C., L. *et al.*, 1996, *Proc. Natl. Acad. Sci. U S A*, 93:14536-41; Sepp-Lorenzino *et al.*, 1995, *J. Biol. Chem.* 270:16580-16587), and some of these substrates have been shown to be degraded by a ubiquitin-dependent process in the proteasome (Schneider, C., L., *supra*; Sepp-Lorenzino, L., *et al.*, 1995, *J. Biol. Chem.*, 270:16580-16587; Whitesell, L. *et al.*, 1994, *Proc. Natl. Acad. Sci. USA*, 91: 8324-8328).

This substrate destabilization occurs in tumor and nontransformed cells alike and has been shown to be especially effective on a subset of signaling regulators, *e.g.*, Raf (Schulte, T. W. *et al.*, 1997, *Biochem. Biophys. Res. Commun.* 239:655-9; Schulte, T. W., *et al.*, 1995, *J. Biol. Chem.* 270:24585-8), nuclear steroid receptors (Segnitz, B., and U. Gehring. 1997, *J. Biol. Chem.* 272:18694-18701; Smith, D. F. *et al.*, 1995, *Mol. Cell. Biol.* 15:6804-12), *v-src* (Whitesell, L., *et al.*, 1994, *Proc. Natl. Acad. Sci. U S A* 91:8324-8328) and certain transmembrane tyrosine kinases (Sepp-Lorenzino, L. *et al.*, 1995, *J. Biol. Chem.* 270:16580-16587) such as EGF receptor (EGFR) and Her2/Neu (Hartmann, F., *et al.*, 1997, *Int. J. Cancer* 70:221-9; Miller, P. *et al.*, 1994, *Cancer Res.* 54:2724-2730; Mimnaugh, E. G., *et al.*, 1996, *J. Biol. Chem.* 271:22796-801; Schnur, R. *et al.*, 1995, *J. Med. Chem.* 38:3806-3812). The ansamycin-induced loss of these proteins leads to the selective disruption of certain regulatory pathways and results in growth arrest at specific phases of the cell cycle (Muisse-Heimericks, R. C. *et al.*, 1998, *J. Biol. Chem.* 273:29864-72), and apoptosis of cells so treated (Vasilevskaya, A. *et al.*, 1999, *Cancer Res.*, 59:3935-40).

Growth arrest of this sort, provided it can be made selective, has important ramifications for the treatment of certain proliferative disorders, including cancer. Whereas cancer treatments have thus far been limited to traditional surgical removal, radiation, and/or chemotherapy, and

whereas these procedures have been more or less successful, a need remains to develop additional therapies with increased efficacy and decreased side-effects that can be used alone or in combination with existing therapies. There particularly remains a need for cancer treatments that target specific cancer types. The present invention satisfies these needs and provides related advantages as well.

Summary of the Invention

Applicants report that many proliferative disorders are associated with aberrant proteins that exhibit a dependence on HSP90. In some cases this dependence manifests as a heightened sensitivity to HSP90 inhibitors such that affected cells can be selectively treated using a dosage that is effective against the aberrant cells but which is ineffective or less effective against normal cells. The aberrant proteins may also exhibit increased proteasome-dependent degradation when in the presence of HSP90 inhibitors. While the invention is not limited by mechanism, increased dependence, sensitivity, and /or disposition to preferential degradation may advantageously be used to treat corresponding proliferative diseases according to the methods of the invention.

Among others, the invention targets two groups of aberrant proteins in particular and the corresponding proliferative disorders they are associated with. Within the first group are fusion proteins generated as a result of non-random chromosomal aberrations (such as translocations, deletions and inversions) that juxtapose parts of the coding sequences of two normal cellular proteins (Rabbitts, T., 1994, *Nature* 372:143-149). Duplication of genetic material within a chromosome resulting in a augmented or semi-duplicative transcripts is also a possibility. Within the second group are mutants and isoforms of cellular proteins that override, dominate, or otherwise obscure the natural gene products and their function. For example, mutants and isoforms of p53 family proteins and other tumor suppressor gene products can act as dominant-negative inhibitors of the corresponding normal protein in heterozygous tumor cells (Blagosklonny, M., *et al*, 1995, *Oncogene*, 11:933-939. Other examples include virally-encoded species of certain kinases, such as v-src and other dominantly-acting mutant oncogene products (Uehara, Y. *et al.*, 1985, *supra*).

Accordingly, in a first aspect the invention features a method of treating a patient having a genetically-defined proliferative disease characterized by a non-random chromosomal aberration. This aberration produces or is capable of producing an oncogenic fusion protein. The method in its broadest embodiment includes (a) providing a

cell, tissue, or fluid sample of a patient suspected of having a genetically-defined proliferative disease; (b) identifying in the cell, tissue, or fluid sample one or more characteristics indicative of the proliferative disease; and (c) administering to the patient a pharmaceutically effective amount of an HSP90-inhibiting compound.

5 The patient may be any organism that can manifest a proliferative disease characterized by an oncogenic fusion protein, which disease is responsive to HSP90 inhibitors. Preferably, but not necessarily, the organism is an animal, more preferably a mammal, and most preferably a human.

10 In preferred embodiments, the inhibitory compound is an ansamycin including but not limited to, *e.g.*, geldanamycin, the geldanamycin derivative, 17-AAG, herbimycin A, and/or macbecin. Most preferably, the ansamycin is 17-AAG. These and other ansamycins and methods of preparing them are well-known in the art. *See, e.g.*, US Patents 3,595,955, 4,261,989, 5,387,584, and 5,932,566. Although preferably the compound is an ansamycin, the method may make use of any compound, synthetic or
15 nonsynthetic, that can inhibit HSP90. Preferably, the inhibitor binds the ATP-binding site of HSP90, or an HSP90 homolog. Radicol is a nonsynthetic example of a compound useful in the invention described and claimed herein. Libraries of small molecules, synthetic and/or nonsynthetic exist or can be made according to routine, well-known methods and screened for HSP90 binding and/or inhibitory activity. These molecules with
20 HSP90 binding and/or inhibitory activity are also useful in the methods of the invention.

 In the identifying step of the invention, which is carried out prior to diagnosis where/when there is no previous diagnosis, any technique can be used that can identify or predict a proliferative disorder targetable by HSP90 inhibitors. Especially preferred are antibody-based and nucleic acid hybridization and/or amplification techniques.
25 Immunoprecipitation, western blotting, and immunoblotting are illustrative examples of antibody-based methods. The antibodies may be monoclonal and/or polyclonal. Illustrative examples of nucleic acid hybridization-based techniques involve Southern blotting, northern blotting, and dot-blotting. Illustrative examples of nucleic acid amplification include standard polymerase chain reactions and variations thereof, *e.g.*,
30 reverse transcriptase-PCR (RT-PCR). The latter is especially useful for identifying levels of gene expression. Other techniques such as the ligase chain reaction (LCR) are also

well-known and have the ability to distinguish an aberrant gene (and indirectly a protein product produced therefrom) from a normal one, or at least predict genotype and/or phenotype. Other methods of identification include ligand-binding assays and gel-retardation assays that display characteristic binding affinities and/or mobility profiles for normal and variant proteins. Where the fusion protein is also an enzyme, one can establish and/or measure aberrance by enzymatic activity (or lack thereof). Conventional and derivative karyotyping and cytochemical techniques can also be used to identify a proliferative disorder of the invention prior to administration of HSP90-inhibitors. One such method is fluorescent *in situ* hybridization (FISH).

In some embodiments, the proliferative disease is a hematopoietic disorder including but not limited to one selected from the group consisting of T or B cell lymphomas, chronic myeloid leukemias (CMLs), acute promyelocytic leukemias (APLs), acute lymphoid or lymphoblastic leukemias (ALLs), acute myeloid leukemias (AMLs), non-Hodgkin lymphomas (NHLs), and chronic myelomonocytic leukemias (CMMLs). In other embodiments, the disease is characterized by a solid tumor, preferably including but not limited to papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma, synovial sarcoma. The embodiments are not necessarily mutually exclusive of one another, and treatment of multiple distinct diseases may simultaneously be effected in a given patient, as the invention has broad-spectrum merit against a variety of different proliferative disorders.

Targeted fusion proteins may contain one or more functional domains or portions thereof, e.g., kinases, DNA binding motifs, etc. Such domains are well-known in the art. Figure 1 illustrates several types of these domains, and the specific fusion proteins, genes, and diseases they can be associated with.

Administration may be by a variety of means. In some preferred embodiments, administration is made *ex vivo*, e.g., removing and treating blood or tissue that is thereafter administered back into the patient. Alternatively, or in combination, administration may be intralésional, e.g., administered to the site of a solid tumor, and/or parenteral. These constitute just some of the many different modes of administration that can be used.

Others are described herein.

In other embodiments, the HSP90-inhibiting compound has an IC_{50} that is higher (preferably two-fold, more preferably five-fold, and most preferably ten-fold) for cells that do not have characteristics indicative of the proliferative disorder as compared with those cells that do have such characteristics.

5 In other embodiments, the patient may be tested pre- and/or post-administration for sensitivity and or effect of one or more HSP90 inhibitors. This may be done *in vitro* or *in vivo*.

Numerous non-random chromosomal aberrations exist that are associated with proliferative disorders. These include but are not limited to chromosomal translocations, inversions, and deletions. Duplications also account for some aberrant chromosomes and aberrant resulting gene products. All aberrations can be targeted in various aspects of the invention. Illustrative examples of specific aberrations include those listed in Figure 1, which is adapted from Table 1 of Rabbitts, Nature 372:143-149 (1994), and others including but not limited to: inv14 (q11; q32), t(9; 22)(q34; q11), t(1; 19)(q23; p13.3), t(17; 19)(q22; p13), t(15; 17)(q21-q11-22), t(11; 17)(q23; q21.1), t(4; 11)(q21; q23), t(9; 11)(q21; q23), t(11; 19)(q23; p13), t(X; 11)(q13; q23), t(1; 11)(p32; q23), t(6; 11)(q27; q23), t(11; 17)(q23; q21), t(8; 21)(q22; q22), t(3; 21)(q26; q22), 5(16; 21)(p11; q22), t(6; 9)(p23; q34), 9; 9?, t(4; 16)(q26; p13), inv(2; 2)(p13; p11.2-14), inv(16)(p13q22), t(5; 12)(q33; p13), t(2; 5)(2p23; q35), t(9;12)(q34;p13), del(12p), t(9;22),+8,+Ph,i(17q), t(15;17)(q22;q12), t(11;17)(q23;q12), t(16;16)(p13;q22), inv(16)(p13;q22), t(9;11)(p22;q23), t(1;22)(p13;q13), t(3;3)(q21;q26), inv(3)(q21q26), t(3;5)(q21;q31), t(3;5)(q25;q34), t(7;11)(p15;p15), t(8;16)(p11;p13), t(9;12)(q34;p13), t(12;22)(p13;q13), del(5q), del(7q), del(20q), t(11q23), t(12;21)(p13;q22), t(5;12)(q31;p13), t(1;12)(q25;p13), t(12;15)(p13;q25), t(1;12)(q21;p13), t(12;21)(q13;p32), and t(5;7)(q33;q11.2). These are merely a sampling of the many chromosomal aberrations well-known in the art that give rise to particular proliferative disorders treatable according to the invention. For these and others, *see, e.g.*, the National Center for Biotechnology Information (NCBI) databases, including, *e.g.*, the Online Mendelian Inheritance in Man (OMIM) database and related links to nucleotide and protein sequences. For purposes of the present invention, the underlying genetic sequences affected are for the most part known and/or may be deduced using techniques routine in the art.

Targeted in particularly preferred embodiments of the invention are chromosomal aberrations corresponding to t(9; 22)(q34; q11) that give rise to bcr-abl fusion proteins, chronic myelogenous leukemia (CML) and, in some cases, acute lymphoid or lymphoblastic leukemia (for ALL, *see, e.g.*, Erikson et al., *Heterogeneity of chromosome 22 breakpoint in Philadelphia-positive (Ph+) acute lymphocytic leukemia*, Proc. Nat. Acad. Sci. 83: 1807-1811 (1986))).

In a second aspect, the invention features a method of treating cancerous cells in a heterogeneous population of cells. The heterogeneous population includes both cancerous and noncancerous cells, and the cancerous cells are further characterized by fusion proteins that are not produced in the noncancerous cells. The method includes administering to the heterogeneous population a pharmaceutically effective amount of an HSP90-inhibiting compound. The population may be tested by separation of samples from each population into separate subpopulations, cancerous or noncancerous, *e.g.*, where cultured cells of each are tested in parallel for response and/or susceptibility to an HSP90-inhibitor or candidate inhibitor molecule. Alternatively, the population may be mixed, *e.g.*, in an *ex vivo* procedure in which cells of a patient, *e.g.*, blood, are treated and administered back to the patient or to another individual. This method otherwise tracks the various described and/or claimed embodiments and/or combinations of embodiments of the first aspect.

In a third aspect, the invention features a method of treating a patient having a proliferative disease associated with a mutant protein or cellular protein isoform dependent on HSP90, or which disease is otherwise sensitive to HSP90 inhibitors. The method includes (a) providing a cell, tissue, or fluid sample of a patient suspected of having said proliferative disease; (b) identifying in the cell, tissue, or fluid sample one or more characteristics indicative of a mutant or cellular protein isoform; and (c) administering to the patient a pharmaceutically effective amount of an HSP90-inhibiting compound.

In preferred embodiments, the mutant protein or cellular protein isoform is selected from the group consisting of src, RET, p53, p51, p63, and p73. Most preferably selected are isoforms of p53 selected from N239S, C176R, and R213*, Y236delta, C174Y, M133T, G245D, E258K, 1-293delta, G245C, R248W, E258K, R282W, R175H, R280K,

V143A, R175H, P177S, H178P, H179R, R181P, 238-9delta, G245S, G245D, M246R, R248Q, R249S, R273H, R273C, R273L, and D281Y.

In another preferred embodiment, the proliferative disease to be treated is rheumatoid arthritis.

5 In some embodiments, the mutant protein or cellular protein isoform may give rise to a dominant negative phenotype. In other embodiments, the mutant or cellular protein isoform may give rise to a dominant positive mutant. In either embodiment, the patient may be heterozygous for the normal cellular gene. Other embodiments track those listed for the preceding aspects.

10 In a fourth aspect, the invention features a method of selectively treating cells that express a mutant protein or cellular protein isoform associated with a proliferative disorder and which mutant/isoform is dependent on HSP90, or which disease is otherwise sensitive to HSP90 inhibitors. The method includes (a) providing a population of cells in which at least some of the population express a mutant protein or cellular protein isoform that is
15 dependent on HSP90 or which are otherwise sensitive to HSP90 inhibitors. The method further includes administering to the population a pharmaceutically effective amount of an HSP90-inhibiting compound. The embodiments for this aspect may otherwise track preceding embodiments.

The foregoing aspects contemplate treatment of existing cell proliferative
20 disorders. It is expected that the invention may also find use in prophylactic prevention of various proliferative disorders of the invention. Further, and where appropriate, each of the embodiments discussed above and different combinations thereof, including subgenus and sub-Markush groups, may cross-apply to each of the different aspects of the invention. Further, where sequence listings are provided, the invention may in some aspects
25 contemplate subsequences of the primary sequence listings. Any subsequence within such primary listing is also contemplated for the invention, as well as all allelic variants, and mutant variants and isoforms thereof, as well as corresponding homologs from other organisms and species. Sequences contiguous with and/or in addition to the listed sequences and their above equivalents are also contemplated.

Advantages of the invention include broad-acting treatment or prophylaxis directed to a variety of different proliferative disorders. Other advantages include the efficient and rapid diagnosis and care of patients suffering from proliferative disorders, with minimal apparent adverse effects. Still other advantages, aspects, and embodiments will be
5 apparent from the figures, the detailed description, and the claims.

Brief Description of the Drawings

Figure 1 illustrates various genetically defined diseases characterized by non-random chromosomal aberrations that give rise to oncogenic fusion proteins. These illustrative aberrations, diseases, and fusion proteins are targeted in various embodiments
10 of the invention. Other targeted aberrations, diseases, and fusion proteins may be found in the specification and in sources commonly known in the art, e.g., the NCBI and GenBank databases, and journal literature.

Detailed Description of the Invention

Definitions

15 As used herein and in the claims the following terms have the following meanings:

A “genetically-defined disease” is one with a basis in DNA. Genetically defined diseases of the invention include “cell proliferative disorders” wherein unwanted cell proliferation of one or more subset(s) of cells in a multicellular organism occurs, resulting in harm, for example, pain or decreased life expectancy to the organism. “Cell proliferative disorders” refer to disorders
20 wherein unwanted cell proliferation of one or more subset(s) of cells in a multicellular organism occurs, resulting in harm, for example, pain or decreased life expectancy to the organism. Cell proliferative disorders include, but are not limited to, cancers, tumors, benign tumors, blood vessel proliferative disorders, autoimmune disorders and fibrotic disorders. These disorders are not necessarily independent. For example, fibrotic disorders may be related to, or overlap with,
25 blood vessel disorders, e.g., atherosclerosis (which is characterized herein as a blood vessel disorder that is associated with the abnormal formation of fibrous tissue).

A “non-random chromosomal aberration” is one that occurs with a nonrandom frequency or is selected for in a population of individuals. Chromosomal aberrations of the invention include translocations, i.e., relocation of a fragment of one chromosome onto another

chromosome; inversions, *i.e.*, wherein pieces of a chromosome rotate within the same chromosome, and deletions, *i.e.*, wherein fragments of a chromosome are lost thereby juxtaposing pieces of DNA that previously did not reside immediately beside each other.

5 An “oncogenic fusion protein” is a protein that is non-natural in and of itself but that may contain one or more pieces of other proteins that may or may not naturally occur within a cell. The fusion protein functions by improperly stimulating cell growth, directly or indirectly. In the context of the invention, the term is also associated with a cellular proliferative disease and is preferably encoded by a nucleic acid found in the cell, *e.g.*, as part of a non-random chromosomal aberration. An oncogenic fusion protein may contain domains or portions thereof, *e.g.*, kinases
10 and/or DNA binding proteins that are well known in the art, or else predicted from their structure to behave as such.

A “fusion” may relate to, as appropriate to a given context, a fusion chromosome, an abnormal mRNA transcribed from the fused portion of the chromosome, or a polypeptide product translated from the abnormal mRNA that is transcribed from the fusion chromosome. These
15 fusions may result from chromosomal deletions, insertions, and/or translocations. Domains or portions of different genes and gene products are frequently, although not necessarily always, brought together as a consequence of the fusion event. For example, an intragenic deletion can result in an intragenic fusion and give rise to an abnormal protein lacking a component from a second gene. More frequently it occurs that two genes or portions thereof are juxtaposed more or
20 less, transcribed together as a single transcript, and translated together as a fusion protein bearing contributions from multiple genes or other chromosomal DNA pieces. In such fusions, reading frames can be preserved, *e.g.*, as in preserved functional domains or portions thereof coming from two or more different genes, or else the reading frame can be disrupted, *e.g.*, as in the case of a “missense” or “nonsense” event as these terms are known in the art.

25 By “providing a cell, tissue, or fluid sample of a patient suspected of having said genetically-defined disease” and “identifying one or more characteristics indicative of said disease in or on said cell, tissue, or fluid sample” can mean, although is not limited to the situation where, the sample is withdrawn from the patient in order to perform the analysis or analyses. Many invasive and noninvasive procedures exist, *e.g.*, NMR, ultrasound and other imaging techniques,
30 that can be used to diagnose, at least in part, an illness and its cause. For example, “tagged” antibodies or other ligands with affinity for a fusion protein or chromosomal aberrancy or

aberrancy product of the invention can be used to make the diagnosis and/or assist in treatment according to methods of the invention.

“Characteristics indicative of said disease” may embrace phenotypes or genotypes and may be measured qualitatively or quantitatively by a variety of techniques. The characteristics may be observed with the naked eye or else through the assistance of a machine or other diagnostic technique(s). Exemplary techniques of measurement include but are not limited to immunoreactivity and/or precipitation, PCR, LCR, karyotyping, and fluorescence activated cell sorting (“FACS”) as those terms are known and understood in the art.

“Administering” can be by direct means, *e.g.*, intralesional or by parenteral or peripheral administration to a patient, or else by indirect means, *e.g.*, as by withdrawing a patient’s cells, treating them, and then re-introducing them back into the patient. The latter constitutes an “*ex vivo*” technique.

An “HSP90-inhibiting compound” is one that disrupts the expression, structure, and/or function of an HSP90 chaperone protein and/or a protein that is dependent on HSP90. HSP90 proteins are highly conserved in nature (see, *e.g.*, NCBI accession #'s P07900 and XM 004515 (human α and β HSP90, respectively), P11499 (mouse), AAB2369 (rat), P46633 (chinese hamster), JC1468 (chicken), AAF69019 (flesh fly), AAC21566 (zebrafish), AAD30275 (salmon), O02075 (pig), NP 015084 (yeast), and CAC29071 (frog). There are thus many different HSP90s, all with anticipated similar effect and similar inhibition capabilities. The HSP90 inhibitor used in the methods of the invention may be specifically directed against an HSP90 of the specific host patient or may be identified based on reactivity against an HSP90 homolog from a different species, or an artificial HSP90 variant. The inhibitors used may be ring-structured antibiotics, *e.g.*, benzoquinone ansamycins, or other types of molecules, *e.g.*, antisense nucleic acids and molecules such as radicicol.

An “ansamycin” includes but is not limited to geldanamycin, 17-AAG, herbimycin A, and macbecin. The specific ansamycin 17-AAG stands for 17-allylamino-17-demethoxygeldanamycin. This and other ansamycins that can be used are well-known in the art. *See, e.g.*, U.S. Patent Nos. 3,595,955, 4,261,989, 5,387,584, and 5,932,566. Ansamycins may be synthetic, naturally-occurring, or else derivatives of naturally occurring ansamycins that are prepared using standard chemical derivatization techniques.

A "pharmaceutically effective amount" means an amount which is capable of providing a therapeutic or prophylactic effect. The specific dose of compound administered according to this invention to obtain therapeutic and/or prophylactic effects will, of course, be determined by the particular circumstances surrounding the case, including, for example, the specific compound administered, the route of administration, the condition being treated, the individual being treated, and the tissue or cell type targeted (or not targeted). A typical daily dose (administered in single or divided doses) will contain a dosage level of from about 0.01 mg/kg to about 100 and more preferably 50 mg/kg of body weight of an active compound of this invention. Preferred daily doses generally will be from about 0.05 mg/kg to about 20 mg/kg and ideally from about 0.1 mg/kg to about 10 mg/kg.

A preferred therapeutic effect is the inhibition to some extent of the growth of cells causing or contributing to a cell proliferative disorder. A therapeutic effect will also normally, but need not, relieve to some extent one or more of the symptoms of a cell proliferative disorder other than cell growth or size of cell mass. In reference to the treatment of a cancer, a therapeutic effect refers to one or more of the following: 1) reduction in the number of cancer cells; 2) reduction in tumor size; 3) inhibition (*i.e.*, slowing to some extent, preferably stopping) of cancer cell infiltration into peripheral organs; 3) inhibition (*i.e.*, slowing to some extent, preferably stopping) of tumor metastasis; 4) inhibition, to some extent, of tumor growth; and/or 5) relieving to some extent one or more of the symptoms associated with the disorder.

In reference to the treatment of a cell proliferative disorder other than a cancer, a therapeutic effect refers to either: 1) the inhibition, to some extent, of the growth of cells causing the disorder; 2) the inhibition, to some extent, of the production of factors (*e.g.*, growth factors) causing the disorder; and/or 3) relieving to some extent one or more of the symptoms associated with the disorder.

With respect to viral infections, the preferred therapeutic effect is the inhibition of a viral infection. More preferably, the therapeutic effect is the destruction of cells which contain the virus.

A "cancer" refers to one or more various types of benign or malignant neoplasms. In the case of the latter, these may invade surrounding tissues and may metastasize to different sites, as defined in Stedman's Medical Dictionary 25th edition (Hensyl ed. 1990).

The term "IC₅₀" is defined as the concentration of an HSP90 inhibitor required to achieve killing or other growth inhibition of 50% of the cells of a homogenous cell type population, or of a particular cell type, *e.g.*, cancerous versus noncancerous, over a period of time. The IC₅₀ is preferably, although not necessarily, greater for normal cells than for cells exhibiting a proliferative disorder.

The term "mutant or isoform cellular protein" refers to a variation of a wild-type protein that occurs in a cell and has a particular function. The mutant or isoform cellular protein of the invention preferably associates with or gives rise to a proliferative disorder, *e.g.*, a cancer, whereas the wild-type protein ordinarily does not.

General

As described and claimed herein, ansamycins and other HSP90 inhibitors can be used to treat two important classes of tumor-promoting (oncogenic) human proteins.

1. Oncogenic Fusion Proteins

The first class of target proteins of the invention are fusion proteins generated as a result of non-random chromosomal aberrations (such as translocations, deletions and inversions) that juxtapose parts of the coding sequences of two normal cellular proteins (Rabbitts, T., 1994, *Nature* 372:143-149) leading to the lineage-specific expression of a mutant fusion protein that has biological activities derived from both parent proteins (Barr, F, 1998, *Nat. Genet.* 19:121-124). Without being limiting of the invention, Applicants have discovered that these fusion proteins have a heightened dependence on HSP90 chaperone activity, and/or decreased stability in the presence of HSP90 inhibitors, thus making them selective targets for treatment with HSP90 inhibitors.

a. Bcr-abl as an example

One example of heightened HSP90 dependence and inhibitor sensitivity is observed when chronic myelogenous leukemia (CML) cells harboring the fusion oncoprotein p210-bcr-abl are treated with HSP90 inhibitors. This fusion protein is degraded faster and more completely than wild type c-abl protein (An, W *et al*, 2000, *Cell Growth and Differentiation* 11: 355-360). Further experimental evidence that bcr-abl expressing leukemia cells are more sensitive to HSP90 inhibitors than are closely related bcr-abl-negative leukemia lines is found in Honma, Y *et al*,

1995, *Int. J. Cancer* 60:685-688, where it is reported that the IC_{50} of herbimycin A in six bcr-abl expressing leukemia cell lines averaged 29.3 nM as compared to a mean IC_{50} of 399.3 nM in a panel of four bcr-abl-negative leukemia lines. Illustrative protein and nucleic acid sequences corresponding to embodiments of bcr-abl fusions of the invention include but are not limited to those found in SEQ ID NOs 1-26 and subsequences thereof, which are further discussed below, along with corresponding NCBI accession numbers.

The normal Bcr gene occupies a region of about 135 kb on chromosome 22. It is expressed as mRNAs of 4.5- and 6.7-kb, which apparently encode for the same cytoplasmic 160-kD protein, and contains 23 exons as well as an unusual inverted repeat flanking the first exon. The BCR protein reportedly contains a unique serine/threonine kinase activity and at least two SH2 binding sites encoded in its first exon and a C-terminal domain that functions as a GTPase activating protein for p21(rac) (Diekmann et al., *Nature* 351: 400-402 (1991). Chisoe et al., *Genomics* 27: 67-82 (1995), sequenced the complete BCR gene and greater than 80% of the human ABL gene, which are both involved in the t(9;22) translocation (Philadelphia chromosome) associated with more than 90% of chronic myelogenous leukemia, 25 to 30% of adult and 2 to 10% of childhood acute lymphoblastic leukemia, and rare cases of acute myelogenous leukemia. Comparison of the gene with its cDNA sequence revealed the positions of 23 BCR exons and putative alternative BCR first and second exons. From the sequence of four newly studied Philadelphia chromosome translocations and a review of several other previously sequenced breakpoints, Chisoe et al. found a variety of breakpoints and recombinations sites possible within the genes. Thus, despite the normal chromosomes and genes each being known (9 and 12; bcr and abl), and the fact that combinations of these genes are known to lead to forms of CML and ALL, the precise genetic breakpoint/recombination junctions that lead to these diseases can vary.

This heterogeneity likely also applies to some non bcr-abl chromosomal aberrations of the invention as well. Nevertheless, because the genes and/or chromosomes involved are known to have a part in the disorders, the disorders are said to be "genetically defined."

b. Other oncogenic fusion proteins

Oncogenic fusion proteins in general are thought to be inherently unstable. To the extent these unstable oncogenic fusion proteins make use of HSP90, they are susceptible of the methods claimed herein. Because the fusion genes and their protein products exert overtly oncogenic activity (Deininger, M *et al*, 2000, *Cancer Res.* 60:2049-2055), preferential degradation of these labile proteins induced by HSP90 inhibitors will have therapeutic value in diseases where the fusion protein is expressed. The present invention thus includes treatment of patients with tumors that are dependent upon other oncogenic fusion proteins that arise from non-random genetic aberrations. An illustrative but nonexhaustive list of these tumors is included in Figure 1, adapted from Table 1 of Rabbitts, T., 1994, *Nature* 372:143-149. The list may be supplemented by additional information found, *e.g.*, in Rowley, J, 1999, *Semin. Hematol.* 36:59-72 and other publications known in the art, as well as discussion below.

Myeloid cancers in particular are within the scope of the invention and include chromosomal abnormalities that give rise to oncogenic fusion proteins that drive the growth of chronic myeloid leukemia (CML), chronic myelomonocytic leukemia (CMML), acute myeloid leukemia (AML), acute promyelocytic leukemia (APL), and acute lymphoblastic leukemia (ALL). The following chromosomal aberrancies give rise to some illustrative fusions implicated in various forms of ALL:

t(1:19)(q23:p13) Pro-pre-B acute lymphoblastic leukemia

t(12:21)(p13;q32) Pro-pre-B acute lymphoblastic leukemia

t(9:22)(q34;q11) B or B-myeloid acute lymphoblastic leukemia

t(9:12)(q34:p13) Acute B-lymphoblastic leukemia

del(12p) Acute B-lymphoblastic leukemia

Specific genes and proteins thereof implicated in various ALL forms include the *MLL* gene and the *TEL* gene, which are commonly rearranged in tumors. Rowley, J, *supra*. Each has numerous fusion partners. ETV6 denotes the name of the *TEL* gene product. Fusion of *TEL*/ETV6 to an acyl CoA synthetase, ACS2, results from a t(5;12)(q31;p13) AML event (Yagasaki, F *et al*, 1999, *Genes Chromosomes Cancer* 26:192-202); fusion of *TEL*/ETV6 to ABL-related gene (*ARG*)

results from a t(1;12)(q25;p13) AML event (Iijima, Y *et al*, 2000, *Blood* 95:2126-2131); fusion of TEL/ETV6 to the neurotrophin-3 receptor TRKC results from a t(12;15)(p13;q25) AML event and gives rise to congenital fibrosarcoma (Liu, Q *et al*, 2000, *EMBO J.* 19:1827-1838, Eguchi, M *et al*, 1999, *Blood* 93:1355-1363); fusion of TEL/ETV6 to the aryl hydrocarbon receptor ARNT results from a t(1;12)(q21;p13) event and gives rise to acute myeloblastic leukemia (AML-M2) (Salomon-Nguyen, F *et al*, 2000, *Proc. Natl. Acad. Sci.* 97:6757-6762); and fusion of TEL/ETV6 to AML-1, the DNA-binding subunit of the AML-1/CBF β transcription factor results from a (12;21)(q13;p32) event that can give rise to acute lymphoblastic leukemia (ALL, Shurtleff, SA *et al*, 1995, *Leukemia* 9:1985-1989) and, in some cases, non-Hodgkin's lymphoma (NHL).

Another illustrative fusion within the scope of the invention is the EWS/FLI-1 hybrid protein that is the hallmark of Ewing's sarcoma and the primitive neuroectodermal tumor family (Silvany, *et al*, 2000, *Oncogene* 19:4523-4530).

Yet another illustrative family of fusion proteins within the scope of the invention is the group of fusion proteins arising from chromosomal rearrangements involving the *RET* gene in thyroid cancer (Kolibaba, K, *et al*, 1997, *Biochem. Biophys. Acta* 1333:F217-F248). Rearrangements of *RET*, resulting in juxtaposition of the RET tyrosine kinase domain with one of three 5' sequences (RET-PTC-1, -2 and -3) generate fusion proteins comprising the kinase domain of RET fused to parts of the genes *H4* (RET-PTC-1), *R1a* of cAMP-dependent protein kinase A (RET-PTC-2) and *ELE-1* (RET-PTC-3).

The scope of the present invention also includes cancers and other proliferative diseases, e.g., rheumatoid arthritis, now known or discovered in the future to be characterized by specific chromosomal aberrations giving rise to fusion proteins.

In at least some cases, heterogeneity of breakpoints within the affected chromosomes is possible, thus providing for the possibility of many different DNA fusions and amino acid sequence variations than those specifically listed in the SEQ ID NOs provided, and which can also be formed by the chromosomal rearrangements, e.g., translocations, inversions, deletions, insertion/duplications, etc., so designated. For example, many different abl-bcr gene combinations and corresponding fusion proteins can be designated by the t(9;22)(q34;q11) translocation event, and all—not just those listed below—are included within the purview of the designation, t(9;22)(q34;q11).

Aberrant proteins of the invention, at least in some instances, feature one or more properties of the individual normal parent genes' gene products (normal polypeptide gene product(s), including e.g., functional and structural domains and subportions thereof resulting from transcription and translation of normal parent genes on normal
5 chromosomes) but otherwise lack exact identity and function with the parent genes' protein products. Chromosomal aberrations may give rise to in-frame fusions or frame-shifts, the latter of which can account for missense or nonsense translation of at least a portion of the mRNA, and thereby result in aberrant polypeptide product(s).

Of the SEQ ID NOs discussed herein, some reflect fusion genes, some reflect
10 fusion gene products, e.g., mRNAs and peptides, and some reflect portions of such entities. Still some others reflect recombination "hot spots" in the normal genes that have a general propensity to form a chromosomal aberration. Each of the above sequences may be useful as diagnostic markers in appropriate embodiments of the invention and/or may be characteristic of a given proliferative disorder (or patient exhibiting such and,
15 accordingly, a candidate for treatment according to some methods of the invention.

While the specific sequences discussed are predominantly human in origin, it is understood that other animal "homologs" of the corresponding human sequences are known in the art and are intended to be within the purview of various aspects of the invention. Because HSP90s are also found in plants, plants and plant cells and tissues
20 exhibiting fusion protein products that give rise to undesirable traits may also be treatable in some aspects and embodiments of the invention. The NCBI nucleotide and protein databases are an example of where such sequences can be found. It is also appreciated that the complete human genome and other genomes have been sequenced, and continue to be sequenced at a high rate, thus facilitating the identity of sequences contiguous with
25 those listed herein and homologs thereto.

Further, some of the sequences listed herein may contain errors associated with the logistical complexities of compiling such extensive data, and the true sequences should be interpreted to be within the scope of the invention, either literally or under the doctrine of equivalents, as they are known in the art.

30 As those of ordinary skill will appreciate, allelic variations and different isotype proteins are also possible for some genes, e.g., the product of differential splicing events in

mRNA, and these are likewise considered within the scope of the invention. Further, some of the NCBI and SEQ ID NOs listed below are for wild-type genes, and are included to give an indication of the different chimeric possibilities for the fused counterpart during a chromosomal aberration according to the invention. Should any of the sequences listed below be in error, such should be construed consistent with what is commonly understood in the art—irrespective of how presented in the application.

c. Further Discussion of Illustrative Chromosomal Aberrancies

Convention: where two or more SEQ ID NOs are provided per NCBI accession #, peptide(s) shall be listed first where applicable, followed by corresponding mRNA/cDNA and/or genomic sequence as the case may be. The terms “nucleotide” and “nucleotides” are interchangeable with, and may be symbolized by, “nt.”

t(9; 22)(q34; q11)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S72478, corresponding to SEQ ID NOs 1 and 2, illustrates one aberrant polypeptide/mRNA in a patient having CML and another patient having ALL. The junction for the nucleic acid sequence between the BCR and ABL genes is stated to reside between nucleotides 100 and 101., with 1-100 derived from BCR and 101-140 derived from ABL.

NCBI #M19695 (SEQ ID NO 3) illustrates a nucleic acid sequence identified from a human myelocytic chimeric bcr/chromosome 9 fusion (CML K562 cell line).

NCBI #M30829 (SEQ ID NOs 4 and 5) illustrates a partial bcr/abl fusion protein mRNA.

NCBI #M13096 (SEQ ID NO 6) illustrates a human chimeric bcr/c-abl fusion protein gene characteristic of cell line K562.

NCBI #M30832 (SEQ ID NOs 7 and 8) corresponds to a human bcr/abl fusion protein, partial cds, clone E3 from cell line EM2.

NCBI # AJ131466 (SEQ ID NOs 9 and 10) corresponds to a partial human bcr/abl (major breakpoint) fusion peptide and the underlying nucleic acid encoding it. Nucleotides 1-373 are said to derive from exons 11-14 of the bcr gene, and nucleotides 374-997 are said to derive from exons 2-4 of the abl gene.

5 NCBI # AF192533 (SEQ ID NOs 11 and 12) corresponds to a partial human bcr/abl (major breakpoint) fusion mRNA. Nucleotides 1-289 are said to come from the bcr gene of chromosome 22 and nucleotides 290-305 from the abl gene of chromosome 9.

10 NCBI # AF321981 (SEQ ID NO 13) corresponds to a BCR-ABL fusion transcript e15a2 mRNA sequence. This particular fusion is stated to result from results from a translocation between the 3' portion of the c-ABL oncogene on chromosome 9 and exon 15 of the BCR gene on chromosome 22; t(9;22).

15 NCBI # M17543 (SEQ ID NO 14) corresponds to at least a portion of a Philadelphia chromosome breakpoint cluster region associated with one embodiment of a bcr abl fusion gene. Nucleotides 1-31 are said to be exon 1 and nucleotides 32-63 are said to be intron A.

NCBI # M17542 (SEQ ID NOs 15 and 16) corresponds to a human bcr/abl fusion protein mRNA (product of translocation t(22q11; 9q34)), exons 1 and 2. Nucleotides 1-31 are stated to denote exon 1 and nucleotides 32-63 are stated to denote exon 2.

20 NCBI # M17541 (SEQ ID NOs 17 and 18) corresponds to a human bcr/abl fusion protein mRNA (product of translocation t(22q11; 9q34)), exons 1 and 2. Nucleotides 1-31 are stated to denote exon 1 and nucleotides 32-63 are stated to denote exon 2.

25 NCBI # AB069693 (SEQ ID NOs 19 and 20) denotes a human partial mRNA corresponding to a bcr/abl e8a2 fusion protein. BCR exons 7 (nucleotides 1-53) and 8 (nucleotides 54-194) are joined to ABL intron 1b inverted (nucleotides 195-249) and ABL exon a2 (nucleotides 250-423).

NCBI # AJ131467 (SEQ ID NOs 21 and 22) correspond to a human partial BCR/ABL chimeric fusion peptide and corresponding mRNA. Nucleotides 1-117 denote exon 1 of the bcr gene, nucleotides 118-193 and 194-298 denote exons 12 and 13 of the

bcr gene, and nucleotides 299-472, 473-768, and 769-922 respectively denote exons 2-4 of the abl gene.

NCBI # AF113911 (SEQ ID NOs 23 and 24) correspond to a partial BCR-ABL minor breakpoint peptide (BCR-ABL fusion) mRNA. Nucleotides 1-455 are stated to be from chromosome 22 and nucleotides 456-1079 from chromosome 9.

NCBI # AF251769 (SEQ ID NOs 25 and 26) correspond to a human partial bcr/abl e1-a3 chimeric fusion protein (BCR/ABLe1-a3) mRNA. Nucleotides 1-455 are stated to be from chromosome 22 and nucleotides 456-1079 from chromosome 9.

inv14 (q11; q32)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # X82240 (SEQ ID NOs 27 and 28) correspond to at least a portion of an mRNA for the gene TCL1, which is disrupted in aberrations of the type noted.

NCBI # NM_021966 (SEQ ID NOs 29 and 30) relate to a human T-cell leukemia/lymphoma 1A (TCL1A), mRNA.

NCBI # X82241 (SEQ ID NO 31) relates to a 5' portion of a human TCL1 gene. Nucleotides 496-560 are said to correspond to exon 1.

NCBI # M14198 (SEQ ID NOs 32 and 33) relate to a human chromosome 14 paracentric inversion producing an heavy chain/T-cell receptor J-alpha fusion protein.

NCBI # X03752 (SEQ ID NOs 34 and 35) relate to a human gene for rearranged Ig V(H) are said to encode the IgVH region (108 aa) and nucleotides 324 to 377 are said to encode 18 amino acids of the TCR-J-alpha protein.

NCBI # M12071 (SEQ ID NOs 36 and 37) relates to a human Ig heavy-chain V-region gene (VII family) rearranged to T-cell receptor alpha-chain D-J-sp region (IgT) in an inv(14)(q11; q32), SUP-T1 cell line. Nucleotides 121-166 are said to derive from exon 1 of the IgH gene, nucleotides 167-248 from intron 1 of the IgH gene, nucleotides 249-623 from exon 2 of the IgH gene, and nucleotides 624-675 from intron 2 of the IgH gene.

NCBI # S45947 (SEQ ID NOs 38 and 39) relate to an IgT=T cell specific exon ET-immunoglobulin VH-T cell receptor J alpha fusion [human, T cell lymphoma cell line SUP-T1, mRNA Mutant, 508 nt]. Nucleotides 34-507 are stated to be IgT coding sequence.

5 NCBI # S45207 (SEQ ID NOs 40 and 41) relate to an IgT=T cell specific exon ET-exon EX-immunoglobulin VH-T cell receptor J alpha fusion [human, T cell lymphoma cell line SUP-T1, mRNA Mutant, 616 nt]. Nucleotides 130-616 are stated to be IgT coding sequence.

t(1; 19)(q23; p13.3)

10 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # M31522 (SEQ ID NOs 42 and 43) relate to a human translocation (t1;19) fusion protein (E2A/PRL) mRNA, 3' end.]. Nucleotides 1-1653 are stated to encode a portion of an E2A/PRL fusion protein.

15 **t(17; 19)(q22; p13)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # M95586 (SEQ ID NOs 44 and 45) relate to a human E2A/HLA fusion protein (E2A/HLF) mRNA, complete cds. Nucleotides 31-1755 are said to be coding
20 sequence.

t(15; 17)(q21-q11-22)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S50916 (SEQ ID NOs 46 and 47) relate to a PML-RAR fusion gene
25 {fusion transcript} [human, mRNA Partial, 1284 nt]. . Nucleotides 1-1251 are said to be coding sequence.

NCBI # M73779 (SEQ ID NOs 48 and 49) relate to a human PML-RAR protein (PML-RAR) mRNA, complete cds; coding sequence: nucleotides 67-2460.

NCBI # AJ417079 (SEQ ID NOs 50 and 51) relate to a human partial mRNA for PML/RARA fusion protein (PML/RARA gene); Nucleotides 1-109 derive from exon 6 of PML, nucleotides 110-172 from intron 2 of RARA, and nucleotides 173-296 from exon 3 of RARA.

t(11; 17)(q23; q21.1)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AAB29813 (SEQ ID NO 52) relates to a retinoic acid receptor alpha, RAR alpha(PLZF=zinc finger protein, PLZF-RAR alpha isoform A=fusion protein) {translocation} [human, acute promyelocytic leukemia patient, Peptide Mutant, 858 aa].

NCBI # AAB29814 (SEQ ID NO 53) relates to a PLZF=zinc finger protein(retinoic acid receptor alpha, RAR alpha, RAR alpha 1-PLZF isoform B=fusion protein) {translocation} [human, acute promyelocytic leukemia patient, Peptide Mutant, 277 aa].

t(4; 11)(q21; q23)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # L22179 (SEQ ID NOs 54 and 55) relate to a human MLL-AF4 der(11) fusion protein mRNA, complete cds. Nucleotides 5-6940 are said to be coding sequence.

NCBI # S67825 (SEQ ID NOs 56 and 57) relate to a human ALL1-AF4 fusion protein mRNA, partial cds. Nucleotides 1-585 are said to derive from chromosome 11 and nucleotides 586-832 from chromosome 4.

NCBI # AF024541 (SEQ ID NOs 58 and 59) relate to a human MLL-AF4 fusion protein mRNA, partial cds. The codons are said to start with nucleotide 3.

NCBI # AF031404 (SEQ ID NOs 60 and 61) relate to a human MLL-AF4 fusion protein mRNA, partial cds. Nucleotides 1-305 are said to derive from chromosome 11 and nucleotides 306-741 from chromosome 4. Codons begin with nucleotide 3.

5 NCBI # L04731 (SEQ ID NO 63) relates to a human translocation T(4;11) of the human ALL-1 gene to chromosome 4.

NCBI # AF177237 (SEQ ID NOs 64 and 65) relate to human cell-line MV4-11, MLL/AF4 fusion protein (MLL/AF4) mRNA, partial cds. Nucleotides 1-62 derive from exon 6 of the MLL gene on chromosome 11, and nucleotides 63-450 from exon 5 of the AF4 gene on chromosome 4.

10 NCBI # AF177236 (SEQ ID NOs 66 and 67) relate to a human A1 MLL/AF4 fusion protein (MLL/AF4) mRNA, partial cds. Nucleotides 1-63 are stated to derive from exon 6 of the MLL gene on chromosome 11, and nucleotides 64-450 from exon 5 of the AF4 gene on chromosome 4.

15 NCBI # AF031403 (SEQ ID NO 68) relates to a human MLL/AF4 translocation breakpoint t(4;11)(q21;23). Nucleotides 1-105 are said to derive from exon 5 of MLL, nucleotides 435-508 from exon 6 of MLL, nucleotides 2195-2326 from exon 7 of MLL, nucleotides 2874-2987 from exon 8 of MLL, and nucleotides 3645-6983 from AF4.

20 NCBI # AF177238 (SEQ ID NOs 69 and 70) relate to a human A1 AF4-MLL fusion protein (AF4-MLL) mRNA, partial cds. Nucleotides 1-484 are said to derive from exon 3 of AF4 and nucleotides 485-596 from exon 7 of MLL.

NCBI # AF177239 (SEQ ID NOs 71 and 72) relate to a human cell-line MV4-11 AF4-MLL fusion protein (AF4-MLL) mRNA, partial cds. Nucleotides 1-484 are said to derive from exon 3 of AF4 and nucleotides 485-596 from exon 7 of MLL

25 NCBI # AF397907 (SEQ ID NO 73) relates to a human AF4/MLL translocation breakpoint region. Nucleotides 1-437 are said to derive from intron 3 of AF6, nucleotides 440-631 from intron 6 of MLL, and nucleotides 632-747 from exon 7 of MLL. The breakpoint is approximately nucleotide 438-439, which was undetermined due to GC compressions.

NCBI # AF024543 (SEQ ID NO 74) relates to a human MLL/AF4 translocation breakpoint t(4;11)(q21;q23).

t(9; 11)(q21; q23)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S82034 (SEQ ID NO 75) relates to an MLL-AF9=fusion gene {fusion site} [human, peripheral blood, acute myeloid leukemia FAB type M1 patient UPN 427, mRNA Partial, 60 nt].

t(11; 19)(q23; p13)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S81007 (SEQ ID NO 76) relates to an MLL/ENL=fusion gene {rearranged derivative 11 junction region} [human, leukemic lymphoblasts, T-cell acute lymphoblastic leukemia patient RUPN2, Genomic Mutant, 74 nt]. The authors indicated that the first 34 nt derived from MLL intron 8 on 11q23, and nt 35-74 from the ENL-distal region on 19p13.3

NCBI # S81008 (SEQ ID NO 77) relates to an ENL {rearranged derivative 19 junction region} [human, leukemic lymphoblasts, T-cell acute lymphoblastic leukemia patient RUPN2, Genomic Mutant, 84 nt]. The authors indicated that nt 55-84 derived from MLL gene 3' region on 11q23.

t(X; 11)(q13; q23)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # NM_005938 (SEQ ID NOs 78 and 79) relate to a human myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 7 (MLLT7), mRNA. Nucleotides 183-1688 denote an MLLT7 coding

region, with nucleotides 465-719 and 480-749 corresponding to a forkhead and forkhead domain, and G and C allelic variations possible at nucleotide 1435.

NCBI # X93996 (SEQ ID NOs 80 and 81) relate to a human mRNA for AFX protein. Nucleotides 183-1688 are said to be AFX coding sequence.

5 **t(1; 11)(p32; q23)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AF331760 (SEQ ID NO 82) relates to human clone UPN5379L mRNA sequence (bone marrow acute lymphoblastic FAB L2 type).

10 **t(6; 11)(q27; q23)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S82519 (SEQ ID NOs 83 and 84) relate to a human MLL-AF6 fusion protein mRNA, partial cds, identified in a leukemic patient, and with the breakpoint stated
15 to be approximately between nt 26 and 27.

NCBI # S82521 (SEQ ID NOs 85 and 86) relate to a an MLL-AF6=fusion gene {breakpoint region, clone b} [human, blood, leukemic patient 2, mRNA Partial, 69 nt]. The breakpoint here is said to reside between nt 24 and 25.

NCBI # S82517 (SEQ ID NOs 87 and 88) relate to an MLL-AF6=fusion gene
20 {breakpoint region} [human, blood, leukemia patient 1, mRNA Partial, 69 nt]. The breakpoint here is said to reside between nt 24 and 25.

t(11; 17)(q23; q21)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

25 NCBI # S72604 (SEQ ID NOs 89 and 90) relate to an AF17...ALL-1 {reciprocal translocation} [human, acute myeloid leukemia patient, mRNA Partial Mutant, 3 genes,

228 nt]. Nucleotides 1-88 are said to derive from AF17 and nucleotides 89-228 from ALL-1.

NCBI # (SEQ ID NOs 91 and 92) relate to a human myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, *Drosophila*); translocated to, 6 (MLLT6), mRNA.

5 Nucleotides approximating 22-168 are said to encode a PHD zinc finger motif and nucleotides 2185-2292 (amino acids 729-764) are said to encode a leucine zipper motif, with A and G allelic variations at nt 592 possible.

t(8; 21)(q22; q22)

10 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # (SEQ ID NOs 93 and 94) relate to a human mRNA for AML1-MTG8 fusion protein, complete cds. The coding sequence is said to be nucleotides 1579-3837 and the breakpoint is said to be between nt 2110 and 2111.

15 NCBI # S78158 (SEQ ID NOs 95 and 96) relate to a human AML1-ETO fusion protein (AML1-ETO) mRNA, partial cds. Nucleotides 1-1767 are said to denote the coding sequence.

NCBI # S78159 (SEQ ID NOs 97 and 98) relate to a human AML1-ETO fusion protein (AML1-ETO) mRNA, partial cds. . Nucleotides 1-696 are said to denote the coding sequence and nucleotides 40 and 41 are said to represent the junction point.

20 NCBI # D14822 (SEQ ID NOs 99 and 100) relate to a human chimeric partial mRNA derived from AML1 and MTG8(ETO) gene sequences. Nucleotides 1-101 are said to derive from the AML1 gene on chromosome 21 and nucleotides 102-799 from the MTG8 (ETO) gene on chromosome 8.

25 NCBI # S45790 (SEQ ID NO 101) relates to a AML1/ETO=acute myelogenous leukemia {translocation breakpoint} [human, Genomic Mutant, 237 nt].

NCBI # Z35296 (SEQ ID NO 102) relates to a human AML1/ETO alternative fusion transcript mRNA, 276bp. Nucleotides 1-117 are said to derive from AML1 and 186-276 are said to derive from ETO.

NCBI # D14823 (SEQ ID NOs 103 and 104) relate to a human chimeric mRNA derived from AML1 gene and MTG8(ETO) gene, partial sequence. Nucleotides 1-101 are said to be derived from the AML1 gene on chromosome 21 and nucleotides 102-1446 are said to be derived from the MTG8(ETO) gene on chromosome 8, with the coding
 5 sequence denoted nt 1-757.

t(3; 21)(q26; q22)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S69002 (SEQ ID NOs 105 and 106) relate to a AML1-EVI-1=AML1-
 10 EVI-1 fusion protein {rearranged translocation} [human, leukemic cell line SKH1, mRNA Mutant, 5938 nt]. The author indicated the boundary between AML1 and EVI-1 to be between nt 2138 and 2139, with the coding sequence being 1603-5790.

NCBI # L21756 (SEQ ID NOs 107 and 108) relate to a human acute myeloid leukemia associated protein (AML1/EAP) mRNA, complete cds. Nucleotides 1-786 are
 15 said to denote the coding sequence.

NCBI # S76343 (SEQ ID NO 109) relates to AML1...EAP {translocation breakpoint} [human, chronic myelogenous leukemia in blast crisis patient, Genomic Mutant, 3 genes, 470 nt]. Nucleotides 1-125 are said to derive from AML1 and nucleotides 126-470 are said to derive from EAP.

20 t(16; 21)(p11; q22)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S71718 (SEQ ID NOs 110 and 111) relate to a TLS/FUS...ERG {translocation} [human, myeloid leukemia patient, peripheral blood, bone marrow cells,
 25 mRNA Partial Mutant, 3 genes, 55 nt]. Nucleotides 46-55 are said to derive from ERG, with the codon start beginning with nt 3.

NCBI # S71805 (SEQ ID NOs 112 and 113) relate to a TLS/FUS...ERG {translocation} [human, myeloid leukemia patient, peripheral blood, bone marrow cells,

mRNA Partial Mutant, 3 genes, 99 nt]. Nucleotides 1-89 are said to derive from TLS/FUS and nucleotides 90-99 from ERG, with the codon start beginning with nt 3.

NCBI # Y10001 (SEQ ID NO 114) relates to a DNA fragment containing fusion point of FUS gene and ERG gene, translocation t(16;21)(p11;q22).

5 **t(6; 9)(p23; q34)**

NCBI # X64229 (SEQ ID NOs 115 and 116) relate to a human dek mRNA. The coding sequence is said to be nt 34-1161.

inv(9;9)

10 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # X63689 (SEQ ID NO 117) relates to a human translocation breakpoint in the "can" gene sequence. The translocation breakpoint is said to be 174..175.

NCBI # M93651 (SEQ ID NOs 118 and 119) relate to a human set gene, complete cds. The coding sequence is said to be 4-837.

15 **t(4; 16)(q26; p13)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

20 NCBI # Z14955 (SEQ ID NOs 120 and 121) relate to a human mRNA encoding the interleukin 2/BCM fusion protein. Nucleotides 1-321 derive from exons 1-3 of IL-2 and nucleotides 322-864 from the BCM gene.

inv(16)(p13q22)

This inversion is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

25 NCBI # AF251768 (SEQ ID NOs 122 and 123) relate to a human PCBFB/MYH11E chimeric fusion protein (CBFB/MYH11) mRNA, partial cds.

Nucleotides 1-41 correspond to exon 5 of CBFB and nucleotides 42-78 to exon 7 of MYH11.

NCBI # AF249898 (SEQ ID NOs 124 and 125) relate to a human PCBFbeta/MYH11A chimeric fusion protein (CBFbeta/MYH11A) mRNA, partial cds.

5 Nucleotides 1-41 correspond to exon 5 of CBFB and nucleotides 42-102 to exon 12 of MYH11.

NCBI # AF249897 (SEQ ID NOs 126 and 127) relate a human PCBFb-MYH11d chimeric fusion protein (CBFB/MYH11D) mRNA, partial cds. Nucleotides 1-41 correspond to exon 5 of CBFB and nucleotides 42-109 to exon 8 of MYH11.

10 NCBI # AF390860 (SEQ ID NO 128) relates to a human isolate UPN2 CBFB/MYH11 translocation breakpoint region sequence.

NCBI # AF390859 (SEQ ID NO 129) relates to a human isolate UPN1 CBFB/MYH11 translocation breakpoint region sequence.

15 NCBI # AF202996 (SEQ ID NOs 130 and 131) relate to human core binding factor beta-smooth muscle myosin heavy chain fusion protein (CBFB-MYH11) mRNA, partial cds. Nucleotides 1-46 are said to correspond to 16q22 and nucleotides 47-89 to 16p13. Nucleotide 50 is said to be a "t" in some cases.

t(5; 12)(q33; p13)

20 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # NM_001987 (SEQ ID NOs 132 and 133) relate to a human ets variant gene 6 (TEL oncogene) (ETV6), mRNA. Nucleotides 25-1383 are said to correspond to coding sequence, of which nt 136-393 are said to correspond to a sterile alpha motif (SAM) pointed domain, nt 1036-1290 to an erythroblast transformation-specific (Ets)-
25 domain, and wherein allelic variations including "c"s and "t"s at each of nt 798, nt 1541, and nt 1598, and an "a"s and "c"s at each of nt 1822 and 1881.

NCBI # U11732 (SEQ ID NOs 134 and 135) relate to a human ets-like gene (tel) mRNA, complete cds. The coding sequence is said to be from nt 25-1383, and the translocation breakpoint said to occur after nt 487.

t(2; 5)(2p23; q35)

5 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI #14: AF032882 (SEQ ID NO 136) relates to a human anaplastic lymphoma kinase receptor (ALK) and nucleophosmin (NPM) truncated genes at a t(2;5) translocation breakpoint. Nucleotides 1-46 are said to be ALK sequence that is truncated at 3' due to
10 translocation, and nucleotides 1370-1451 are said to be NPM sequence that is truncated at 5' due to translocation.

NCBI # S82740 (SEQ ID NO 137) relates to a NPM/ALK=fusion gene {translocation breakpoint} [human, lymphoma cells SUP-M2, Genomic, 1565 nt].

NCBI # S82725 (SEQ ID NO 138) relates to a NPM/ALK=fusion gene
15 {translocation breakpoint} [human, lymphoma cells SU-DHL-1, Genomic, 1679 nt].

NCBI # U04946 SEQ ID NOs 139 and 140) relate to a human nucleophosmin-anaplastic lymphoma kinase fusion protein (NPM/ALK) mRNA, complete cds. The recombination junction is said to occur at nt 353.

t(11; 22) (q24; q12)

20 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AJ229320 (SEQ ID NO 141) relates to a human translocation t(11;22) DNA in ewings's tumor derivative 22 (isolate: EWTUM64/ MIC). Nucleotides 1-88 are said to denote EWS sequence and nucleotides 89-180 FLI-1 sequence.

25 NCBI # AJ229311 SEQ ID NO 142) relates to a human translocation t(11;22) DNA in ewings's tumor derivative 22 (isolate: EWTUM56/ EW20). Nucleotides 1-114 are said to denote EWS sequence and nucleotides 115-180 FLI-1 sequence.

NCBI # AF177752 (SEQ NO 143) relates to a human clone Jugo Ewing's sarcoma-specific EWS-FLI1 chimera target sequence.

NCBI # AF177751 (SEQ ID NO 144) relates to a human Juyon Ewing's sarcoma-specific EWS-FLI1 chimera target sequence.

5 NCBI # AF177750 (SEQ ID NO 145) relates to a human clone Iti Ewing's sarcoma-specific EWS-FLI1 chimera target sequence.

NCBI # AF327066 SEQ ID NOs 146 and 147) relate to a human Ewings sarcoma EWS-Fli1 (type 1) oncogene mRNA, complete cds.

10 NCBI # XM_060745 (SEQ ID NOs 148 and 149) relate to a human similar to EWS/FLI1 activated transcript 2 (H. sapiens) (LOC127935), mRNA. Nucleotides 10-225 and 13-195 are said to denote src homology 2 (SH2) domains.

NCBI # AF403479 SEQ ID NOs 150 and 151) relate to a human EWS/FLI1 activated transcript 2 protein mRNA, complete cds.

15 NCBI # AF020264 (SEQ ID NOs 152 and 153) relate to a human EWS/FLI1 activated transcript 2 homolog (EAT-2) gene, partial cds.

NCBI # AF020263 (SEQ ID NOs 154 and 155) relate to a Mus musculus EWS/FLI1 activated transcript 2 (EAT-2) mRNA, complete cds.

20 NCBI # S72620 SEQ ID NOs 156 and 157) relate to a EWS...Fli1 [human, T93-113 tumor, mRNA Partial Mutant, 3 genes, 229 nt]. Nucleotides 1-85 are said to denote partial EWS gene sequence and nt 86-229 are said to denote partial FLI-1 sequence.

NCBI # S64709 (SEQ ID NO 158) relates to EWS...Fli-1 {translocation} [human, IARC-EW11 Ewing's tumor-derived cells, mRNA Mutant, 3 genes, 100 nt]. Nucleotides 1-18 are said to denote partial EWS gene sequence and nt 19-100 are said to denote partial FLI-1 sequence.

25 NCBI # S62665 (SEQ ID NOs 159 and 160) relate to a type 4 EWS-FLI1 fusion {translocation} [human, primitive neuroectodermal tumor cell line TC-32, mRNA Partial Mutant, 60 nt]. Positions 1-31 are said to be from the 5' portion of EWS on chromosome

22 and positions 32-60 are said to be from the 3' (DNA-binding) region of FLI1 on chromosome 11.

inv(10)(q11.2; q21)

This aberration is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AF395885 (SEQ ID NO 161) relates to a human H4/RET fusion mRNA, partial sequence. tyrosine kinase domain of the ret. Nt 1-83 are said to derive from H4, nt 84-142 from an unidentified insertion sequence, and nt 143-447 from ret. The tyrosine kinase domain in the ret portion is said be constitutively active in the fusion product.

NCBI # NM_005436 (SEQ ID NOs 162 and 163) relate to a human DNA segment, single copy, probe pH4 (transforming sequence, thyroid-1, (D10S170), mRNA. Nt 37-1794 are said to represent coding sequence, nt 202-996 said to encode a myosin tail, nt 610-999 an Ezrin/radixin/moesin family (ERM) region, with "a" and "c" allelic variation possible at nts 979, 1080, and 1445, and "a" and "g" possible at nt 1362, and "t" and "c" possible at nts 1996 and 2642.

NCBI # S77910 (SEQ ID NO 164) relates to H4= gene frequently rearranged with the ret proto-oncogene {promoter} [human, Genomic, 447 nt]. Nt 442-447 are said to correspond to the coding sequence, "MA".

NCBI # S72869 (SEQ ID NOs 165 and 166) relate to H4(D10S170)=putative cytoskeletal protein [human, thyroid, mRNA, 3011 nt]. Nt 37-1794 are said to correspond to coding sequence.

NCBI # X65617 (SEQ ID NO 167) relates to a human ret proto-oncogene DNA. Nt 1-54 are said to replace sequences from the H4 gene, nt 55-787 are said to correspond to an intron between the transmembrane and tyrosine kinase domain, and nt 788-808 said to correspond to an exon coding for a tyrosine kinase domain.

t(12;22)(q13;q12)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # NM_005171 (SEQ ID NOs 168 and 169) relate to a human activating transcription factor 1 (ATF1), mRNA. Nt 157-252 are said to correspond to a pKID domain and nt 631-795 are said to correspond to a bZIP transcription factor region.

NCBI # AF047022 (SEQ ID NOs 170 and 171) relate to a human RNA binding protein-activating transcription factor-1 fusion protein (EWS-ATF1) mRNA, partial cds. Nt 1-65 are said to correspond to chromosome 22 and nt 66-353 to chromosome 12, with nt 66^67 said to represent the fusion junction between the EWS and ATF1 genes.

t(12; 16(q13; p11))

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AJ301614 (SEQ ID NO 172) relates to a human t(12;16)(q13;p11) translocation breakpoint (CHOP/FUS chimaeric genomic DNA). Nt 1-225 are said to correspond to the CHOP gene (chromosome 12) and nt 226-500 to the FUS gene (chromosome 16).

NCBI # AJ301613 (SEQ ID NO 173) relates to a human t(12;16)(q13;p11) translocation breakpoint (FUS/CHOP chimaeric genomic DNA). Nt 1-317 are said to correspond to the FUS gene (chromosome 16) and nt 318-521 to the CHOP gene (chromosome 12).

NCBI # AJ301612 (SEQ ID NOs 174 and 175) relate human partial mRNA for FUS/CHOP chimaeric fusion protein (type 9 transcript variant). Nt 1-118 are said to originate from chromosome 16 and nt 119-225 are said to originate from chromosome 12.

NCBI # AJ301611 (SEQ ID NOs 176 and 177) relate to a human partial mRNA for FUS/CHOP chimaeric fusion protein (type 8 transcript variant). Nt 1-128 are said to originate from chromosome 16 and nt 129-235 are said to originate from chromosome 12.

NCBI # NM_004960 (SEQ ID NOs 178 and 179) relate to a human fusion protein derived from t(12;16) malignant liposarcoma (FUS), mRNA. Nt 79-1659 are said to denote the coding sequence. Allelic variation is stated to be possible at nts 225 (a/c), 369 (c/t), and 1586 (a/g). Nt 937-1173 are said to denote an RNA recognition motif

(RRM), and nt 1354-1425 are said to denote a zinc finger domain in a Ran binding proteins (zf-Ranbp).

NCBI # S75762 (SEQ ID NOs 180 and 181) relate to a FUS...CHOP [human, myxoid liposarcoma specimens, mRNA Partial Mutant, 3 genes, 652 nt]. Nucleotides 1-272 are said to derive from FUS.

NCBI #X71427 (SEQ ID NOs 182 and 183) relate to a human mRNA for FUS-CHOP protein fusion. Nucleotides 70-1458 are said to denote the fusion coding sequence.

NCBI # X71428 (SEQ ID NOs 184 and 185) relate to a human mRNA for FUS glycine rich protein. Nucleotides 73-1650 are said to denote the coding sequence.

NCBI # Y10004 (SEQ ID NO 186) relates to a human DNA fragment containing fusion point of FUS gene and CHOP gene, translocation t(12;16)(q13;p11). The sequence is said to contain 5'-FUS intron 7 sequence and intron 1 3' sequence from CHOP.

NCBI # Y10003 (SEQ ID NO 187) relates to a human DNA fragment containing fusion point of FUS gene and CHOP gene, translocation t(12;16)(q13;p11). The sequence is said to contain 5'-FUS intron 7 sequence and intron 1 3' sequence from CHOP.

NCBI # Y10002 (SEQ ID NO 188) relates to a human DNA fragment containing fusion point of FUS gene and CHOP gene, translocation t(12;16)(q13;p11). The sequence is said to contain 5'-FUS intron 7 sequence and intron 1 3' sequence from CHOP.

NCBI # S75763 (SEQ ID NOs 189 and 190) relate to a FUS...CHOP [human, myxoid liposarcoma specimens, mRNA Partial Mutant, 3 genes, 377 nt]. Nt 1-272 are said to derive from FUS and nt 273-377 from CHOP.

t(2; 13)(q35;q14)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # U02308 (SEQ ID NOs 191 and 192) relate a human PAX-3-FKHR gene fusion mRNA, partial cds. Nt 1-2070 are said to be coding sequence.

t(x; 18)(p11.2; q11.2)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S79894 (SEQ ID NOs 193 and 194) relate to a SYT...SSX {translocation
 5 breakpoint} [human, synovial sarcoma patient, tumor, mRNA Mutant, 3 genes, 165 nt].
 Nt 1-18 are said to derive from SYT and nt 22-165 from SSX.

NCBI # X86175 (SEQ ID NOs 195 and 196) relate to a human mRNA for SSX2 protein. Nt 92-658 are said to be coding sequence.

10 The following chromosomal aberrations are not discussed in Figure 1 and will now be discussed in more detail:

t(12:21)(p13;q32)

The TEL (ETV6)-AML1 (CBFA2) gene fusion is the most common reciprocal chromosomal rearrangement in childhood cancer, occurring in approximately 25% of the most predominant subtype of leukemia- common acute lymphoblastic leukemia. Ford et
 15 al., Proc. Natl. Acad. Sci. U.S.A. 95 (8), 4584-4588 (1998), reported characterization of the translocation event responsible for one TEL-AML1 genomic sequence in a pair of monozygotic twins diagnosed at ages 3 years, 6 months and 4 years, 10 months with common acute lymphoblastic leukemia. The twins shared an identical rearranged IgH allele. These data have implications for the etiology and natural history of childhood
 20 leukemia.

Other articles of interest on this subject include: Wiemels et al., *Protracted and variable latency of acute lymphoblastic leukemia after TEL-AML1 gene fusion in utero*, Blood. 1999 Aug 1;94(3):1057-62; Rubnitz et al., *The role of TEL fusion genes in pediatric leukemias*, Leukemia, 1999 Jan;13(1):6-13. Review; Romana et al., *The t(12;21) of acute lymphoblastic leukemia results in a tel-AML1 gene fusion*, Blood. 1995 Jun
 25 15;85(12):3662-70; Seeger et al., *TEL-AML1 fusion in relapsed childhood acute lymphoblastic leukemia*, Blood. 1999 94(1):374-6; Bayar et al., *Monozygotic twins with congenital acute lymphoblastic leukemia (ALL) and t(4;11)(q21;q23)*, Cancer Genet Cytogenet. 1996 Jul 15;89(2):177-80; Kobayashi et al., *Detection of the Der (21)t(12;21)*

chromosome forming the *TEL-AML1* fusion gene in childhood acute lymphoblastic leukemia, *Leuk Lymphoma*. 1997 Dec;28(1-2):43-50; and Shurtleff et al., *TEL/AML1 fusion resulting from a cryptic t(12;21) is the most common genetic lesion in pediatric ALL and defines a subgroup of patients with an excellent prognosis*, *Leukemia*, 1995 (12):1985-9.

NCBI# AF044317 (SEQ ID NO 197) relates to a human TEL/AML1 fusion gene, partial sequence. This was derived from an ALL infant. Nts 1-407 are said to derive from TEL and nts 408-548 from AML-1.

NCBI # AF231770 (SEQ ID NO 198) relates to a human ETV6/AML1 translocation breakpoint region.

t(9;12)(q34; p13)

In human leukemia, activation of the ABL proto-oncogene locus on chromosome 9 most commonly occurs as a result of its fusion to the BCR locus on chromosome. Papadopoulos et al., *Cancer Res.* 55 (1), 34-38 (1995), reported a t(9;12) event—a chimeric ABL protein displaying an elevated tyrosine kinase activity fused to a TEL protein from chromosome 12. Like BCR, TEL is fused in-frame with ABL and produces a fusion protein with an elevated tyrosine kinase activity when assayed in an immune complex. The amino-terminal sequences of TEL encodes a helix-loop-helix motif which may mediate dimerization. 43: *See also* Okuda et al., *Oncogene*. 1996 Sep 19;13(6):1147-52.

NCBI # Z36279 (SEQ ID NO 199) relates to a human (9TX) breakpoint position DNA for the tel-abl fusion identified by Papadopoulos et al. The translocation breakpoint is said to reside between nt 567 and 568.

del(12p)

Revy et al., *Cell* 102:565-575 (2000), reported hyper IgM immunodeficiencies associated with deletions of 19 and 9 bases at cDNA positions 21 and 175 respectively of the activation-induced cytidine deaminase (AID) gene. The former results in a 6 amino acid deletions and a phe15 to ter premature nonsense codon. The latter results in a 3-amino acid deletion and leu59-to -phe substitution.

NCBI # AB040430 (SEQ ID NOs 200 and 201) relate to a human AID gene for activation-induced cytidine deaminase, complete cds.

NCBI # AB040431 (SEQ ID NO 202 and 203) relate to a human AID mRNA for activation-induced cytidine deaminase, complete cds. Nt 77-673 is said to be coding
5 sequence.

NCBI # NM_020661 (SEQ ID NOs 204 and 205) relate to a human activation-induced cytidine deaminase (AICDA), mRNA. Nt 77-673 is said to be coding sequence. Allelic variation (a/g) is said to occur at nt 541.

t(15;17)(q22;q12)

10 de The et al., Cell 1991 Aug 23;66(4):675-84, reported a PML-RAR alpha fusion mRNA generated by a t(15;17) translocation associated with acute promyelocytic leukemia (APL). The gene product contained a novel zinc finger motif common to several DNA-binding proteins and the mRNA encoded a predicted 106 kd chimeric protein containing most of the PML sequences fused to a large part of RAR alpha, including its
15 DNA- and hormone-binding domains. In transient expression assays, the hybrid protein exhibited altered transactivating properties if compared with the wild-type RAR alpha progenitor. Identical PML-RAR alpha fusion points were found in several patients, suggesting that in APL the t(15;17) translocation generates an RAR mutant that could contribute to leukemogenesis through interference with promyelocytic differentiation.

20 NCBI # S50916 (SEQ ID NOs 206 and 207) relate to a PML-RAR fusion gene {fusion transcript} [human, mRNA Partial, 1284 nt]. Nt 1-1251 is said to be coding sequence.

NCBI # M73779 (SEQ ID NOs 208 and 209) relate to a human PML-RAR protein (PML-RAR) mRNA, complete cds. Nt 67-2460 is said to be coding sequence.

25 NCBI # AJ417079 (SEQ ID NOs 210 and 211) relate to a human partial mRNA for PML/RARA fusion protein (PML/RARA gene). Nt 1-109 are said to derive from exon 6 of PML and nts 110-172 and 173-296 are said to derive from intron 2 and exon 3 of RARA.

t(11;17)(q23;q12)

Chen et al., EMBO J., 12 (3), 1161-1167 (1993), reported a fusion between a novel Kruppel-like zinc finger gene and the retinoic acid receptor-alpha locus due to a variant t(11;17) translocation associated with acute promyelocytic leukaemia (APL). Chen et al identified mRNAs containing the coding sequences of the new gene, fused in-frame either upstream of the RAR alpha B region or downstream from the unique A1 and A2 regions of the two major RAR alpha isoforms. The new gene, which Chen et al. termed PLZF (for promyelocytic leukaemia zinc finger), encodes a potential transcription factor containing nine zinc finger motifs related to the Drosophila gap gene Kruppel and is expressed as at least two isoforms which differ in the sequences encoding the N-terminal region of the protein. Within the haematopoietic system the PLZF mRNAs are detected in the bone marrow, early myeloid cell lines and peripheral blood mononuclear cells, but not in lymphoid cell lines or tissues. In addition, the PLZF mRNA levels were down-regulated in NB-4 and HL-60 promyelocytic cell lines in response to retinoic acid-induced granulocytic differentiation and were very low in mature granulocytes, suggesting an important role for PLZF as well as retinoic acid and its receptors in myeloid maturation.

NCBI # NM_006006 (SEQ ID NOs 212 and 213) relate to a human zinc finger protein 145 (Kruppel-like, expressed in promyelocytic leukemia) (ZNF145), mRNA. Nt 76-2097 are said to be coding sequence.

NCBI # Z19002 (SEQ ID NOs 214 and 215) relate to a human PLZF gene encoding kruppel-like zinc finger protein. Nt 76-2097 are said to be coding sequence.

t(16;16)(p13;q22) and inv(16)

Springall et al., Leukemia 12 (12), 2034-2035 (1998), identified a novel CBFβ-MYH11 fusion transcript in a patient with AML and attributed it to an inversion/translocation of chromosome 16. *See also*, Krauter et al., Genes Chromosomes Cancer. 2001 Apr;30(4):342-8, *Detection and quantification of CBFβ/MYH11 fusion transcripts in patients with inv(16)-positive acute myeloblastic leukemia by real-time RT-PCR*; Martinelli et al., Haematologica. 2000 May;85(5):552-5, *Long-term disease-free acute myeloblastic leukemia with inv(16) is associated with PCR undetectable CBFβ/MYH11 transcript*; and Dierlamm et al., Genes Chromosomes Cancer. 1998

Jun;22(2):87-94. Review, *FISH identifies inv(16)(p13q22) masked by translocations in three cases of acute myeloid leukemia.*

NCBI # AF202996 (SEQ ID NOs 216 and 217) relate to a human core binding factor beta-smooth muscle myosin heavy chain fusion protein (CBFB-MYH11) mRNA, partial cds. Nt 1-46 are said to originate from 16q22 and nt 47-89 are said to originate from 16p13. Nt 50 is said to be a "t" in some reports.

NCBI # AF251768 (SEQ ID NOs 218 and 219) relate to human PCFBF/MYH11E chimeric fusion protein (CBFB/MYH11) mRNA, partial cds. Nt 1-42 are said to derive from exon 5 of CBFB and nts 42-78 from exon 7 of MYH11.

NCBI # AF249898 (SEQ ID NOs 220 and 221) relate to a human PCBFbeta/MYH11A chimeric fusion protein (CBFbeta/MYH11A) mRNA, partial cds. Nt 1-42 are said to derive from exon 5 of CBFB and nts 42-78 from exon 12 of MYH11.

NCBI # AF249897 (SEQ ID NOs 222 and 223) relate to a human s PCBFb-MYH11d chimeric fusion protein (CBFB/MYH11D) mRNA, partial cds.

NCBI # AF390860 (SEQ ID NO 224) relates to a human UPN2 CBFB/MYH11 translocation breakpoint region sequence.

NCBI # AF390859 (SEQ ID NO 225) relates to a human isolate UPN1 CBFB/MYH11 translocation breakpoint region sequence.

t(9;11)(p22;q23)

Tkachuk et al., Cell 71: 691-700, (1992), showed that the gene involved in recurring 11q23 leukemogenic translocations codes for an unusually large protein that is a homolog of Drosophila 'trithorax' and is involved in homeotic gene regulation (MLL; aka ALL1). In studies of a t(11;19) translocation, they identified a chimeric protein containing the amino-terminal 'AT-hook' motifs of the MLL gene on chromosome 11 fused to a previously undescribed protein from chromosome 19. The nucleotide sequence determinations demonstrated an open reading frame that coded for a predicted 62-kD protein, which Tkachuk et al. named ENL.

Nakamura et al., Proc. Nat. Acad. Sci. 90: 4631-4635, (1993), showed that the gene on chromosome 19 that is fused to the MLL gene in patients with leukemia and translocation t(11;19)(q23;p13) shows high sequence homology to the genes on chromosome 4 and chromosome 9 that are fused with the ALL1 gene in patients with translocation t(4;11)(q21;q23) and t(9;11)(p22;q23), respectively. The 3 protein gene products contained nuclear targeting sequences as well as serine-rich and proline-rich regions. The results suggested that the different proteins fused to ALL1 polypeptides. These leukemias provide similar functional domains.

Negrini et al., Cancer Res 1993 Oct 1;53(19):4489-92, reported potential topoisomerase II DNA-binding sites at the breakpoints of a t(9;11) chromosome translocation in acute myeloid leukemia. The event examined was a t(9;11)(p22;q23) chromosome translocation and the breakpoints on the two chromosomes occurred within introns of the involved genes: AF-9 on chromosome 9, and ALL-1 on chromosome 11. Sequence analysis identified heptamers flanking the breakpoints on both chromosomes 9 and 11, suggesting that the V-D-J recombinase was involved in the translocation. See also Cimino et al., Cancer Res. 1991 Dec 15;51(24):6712-4, *Cloning of ALL-1, the locus involved in leukemias with the t(4;11)(q21;q23), t(9;11)(p22;q23), and t(11;19)(q23;p13) chromosome translocations.*

Poirel et al., Blood 87 (6), 2496-2505 (1996), reported an MLL-AF9=fusion gene {fusion site} [human, peripheral blood, acute myeloid leukemia FAB type M1 patient UPN 427, mRNA Partial, 60 nt]; NCBI # S82034 (SEQ ID NO 226), and indicated the breakpoint to be at nucleotide 29.

t(1;22)(p13;q13)

Nakamura et al., Proc Natl Acad Sci U S A 1993 May 15;90(10):4631-5, correlated aberrations on chromosomes 4, 9, and 19 involved in 11q23 abnormalities in acute leukemia with shared sequence homology and/or common motifs, including fusions of the ENL gene with ALL-1 in (11;19) translocations. ENL proteins contain nuclear targeting sequences as well as serine-rich and proline-rich regions. Stretches abundant in basic amino acids are also present.

NCBI # AF364037 (SEQ ID NOs 227 and 228) relate to a human megakaryoblastic leukemia-1 protein/RNA-binding motif protein 15s + ae fusion protein (MKL1/RBM15 fusion) mRNA, complete cds. Ma et al., Nat. Genet. 28 (3), 220-221 (2001) identified this with an acute megakaryoblastic leukemia patient. Nt 144-221 are said to be coding sequence, with nts 1-150 deriving from chromosome 22 and nts 151-300 deriving from chromosome 1.

t(3;3)(q21;q26) or inv(3)(q21q26)

Ogawa et al., Oncogene 1996 Jul 4;13(1):183-91 showed that overexpression of the Evi-1 gene appears to be a consistent feature of the 3q21q26 syndrome, an association of myeloid leukemias/myelodysplastic syndrome with a specific chromosomal aberration involving both 3q21 and 3q26, such as t(3;3)(q21;q26) or inv(3)(q21q26). The rearrangement in 3q26 has been reported to occur near the Evi-1 locus, implicating that it is the critical gene deregulated in the 3q21q26 syndrome. Ogawa identified a structural abnormality of Evi-1 protein in a case with the 3q21q26 syndrome. That case carried the typical inv(3)(q21q26), in which the 3q26 breakpoint is located within an intron of the Evi-1 gene, and resulted in overexpression of a normally unexpressed, aberrant form of Evi-1 protein, in which the C-terminal 44 amino acids of wild-type Evi-1 protein were truncated and replaced by five amino acids. The truncated Evi-1 protein was shown to increase AP1 activity when expressed in NIH3T3 cells as its wild-type counterpart. The origin of this peculiar type of rearrangement of the Evi-1 gene was shown not to be an artifact during establishment of the cell line, but rather an event that occurred in the primary leukemic cells, and consistent with 3q21q26 syndrome.

NCBI # S82592 (SEQ ID NOs 229 and 230) relate to an Evi-1=Evi-1 protein {3' region, deletion region} [human, megakaryoblastoid cell line MOLM-1, chronic myelocytic leukemia patient, mRNA Partial Mutant, 916 nt]. Nt 1-132 are said to represent a partial coding sequence.

t(3;5)(q25;q34)

Yoneda-Kato et al., Oncogene 12: 265-275 (1996), showed that t(3;5)(q25.1;q34) of myelodysplastic syndrome and acute myeloid leukemia produces a novel fusion gene, NPM-MLF1, which results from an in-frame fusion between the 5-prime coding region of

the nucleophosmin gene on chromosome 5 and a gene on chromosome 3, designated MLF1 (myeloid leukemia factor-1). The translocation was identified in 3 t(3;5)-positive cases of AML. Expression of the mRNA was widespread but highest in testis, ovary, skeletal muscle, heart, kidney and colon. Antibodies to MLF1 detected a 31-kD protein in K562 and HEL erythroleukemia cell lines

NCBI # L49054 (SEQ ID NOs 231 and 232) relate to a t(3;5)(q25.1;p34) fusion gene NPM-MLF1 mRNA, complete cds. Nt 109-915 are said to be coding sequence.

NCBI # BC007045 (SEQ ID NOs 233 and 234) relate to a human myeloid leukemia factor 1, clone MGC:12449, mRNA, complete cds. Nt 107-913 are said to be coding sequence.

NCBI # L49054 (SEQ ID NOs 235 and 236) relate to a human t(3;5)(q25.1;p34) fusion gene NPM-MLF1 mRNA, complete cds. Nt 109-915 are said to be coding sequence.

t(7;11)(p15;p15)

Borrow et al., Nat. Genet. 1996 Feb;12(2):159-67, reported a t(7;11)(p15;p15) translocation in acute myeloid leukaemia that fused the genes for nucleoporin NUP98 and class I homeoprotein HOXA9.

NCBI # U41814 (SEQ ID NOs 237 and 238) relate to human NUP98-HOXA9 fusion protein mRNA, partial cds. Nt 46^47 are said to represent a NUP98-HOXA9 in-frame junction and nt 138^139 are said to be an alternative splice site within HOXA9

NCBI # NM_002142 (SEQ ID NOs 239 and 240) relate to a human homeo box A9 (HOXA9), mRNA. Nts 67 and 213 are said to have allelic variation possible (c/g), and nt 397-567 and 397-576 are said to respectively represent a homeobox domain and a homeodomain (HOX region).

NCBI # U81511 (SEQ ID NOs 241, 242, and 243) relate to a human HOXA-9A and HOXA-9B (HOXA-9) gene, alternatively spliced, complete cds. Nts 145-502, 4327-4894, and 5893-6131 are said to be exon (coding) sequences, with introns present at 503-5892 and 4895-5892. Alternative splicing events are said to account for the overlap.

t(8;16)(p11;p13)

Panagopoulos et al., Genes Chromosomes Cancer. 2000 Aug;28(4):415-24, used RT-PCR analysis to identify MOZ-CBP and CBP-MOZ chimeric transcripts in acute myeloid leukemias with t(8;16)(p11;p13) translocations.

5 NCBI # AJ251844 (SEQ ID NOs 244 and 245) relate to human partial mRNA for MOZ/CBP chimeric transcript type II. Nt 1-188 are said to derive from chromosome 8 and nts 189-415 from chromosome 16.

NCBI # AJ251845 (SEQ ID NOs 246 and 247) relate to a human partial mRNA for CBP/MOZ chimeric transcript. Nt 1-110 are said to derive from chromosome 16 and nts
10 111-229 from chromosome 8.

NCBI # AJ251843 (SEQ ID NOs 248 and 249) relate to human partial mRNA for MOZ/CBP chimeric transcript type I. Nt 1-188 are said to derive from chromosome 8 and nts 189-1128 from chromosome 16.

NCBI # U47742 (SEQ ID NOs 250 and 251) relate to human monocytic leukaemia
15 zinc finger protein (MOZ) mRNA, complete cds.

NCBI # U85962 (SEQ ID NOs 252 and 253) relate to a human CREB-binding protein mRNA, complete cds. Nt 814-8147 are said to contain coding sequence and nts 819-1124 are said to encode a nuclear receptor binding domain.

t(9;12)(q34;p13)

20 Papadopoulos et al., Cancer Res. 1995 Jan 1;55(1):34-8, reported activation of ABL by fusion to an ets-related gene, TEL.

NCBI # Z35761 (SEQ ID NOs 254 and 255) relate to a human TEL/ABL fusion protien. Nt 1-463 are said to contain a partial TEL sequence and nt 464-549 are said to contain ABL sequence.

25 NCBI # Z36279 (SEQ ID NO 256) relates to human (9TX) breakpoint position DNA. The breakpoint position is said to reside at 567..568.

NCBI # Z36278 (SEQ ID NO 257) relates to human (boucher) breakpoint position DNA. The breakpoint position is said to reside at 567..568.

t(12;22)(p13;q13)

Buijs et al., *Oncogene*. 1995 Apr 20;10(8):1511-9, reported that a t(12;22) (p13;q11) event resulted in a myeloproliferative disorders characterized by the fusion of the ETS-like TEL gene on 12p13 to the MN1 gene on 22q11.

NCBI # X85024 (SEQ ID NOs 258 and 259) relate to a human mRNA for TEL-MN1 fusion gene (type II). Nt 22..23 is said to be the fusion site.

NCBI # X85026 (SEQ ID NOs 260 and 261) relate to a human mRNA for a TEL-MN1 fusion gene (type I). Nt 22..23 is said to be the fusion site.

NCBI # X85027 (SEQ ID NOs 262 and 263) relate to a human mRNA for a MN1-TEL fusion gene (type II). Nt 22..23 is said to be the fusion site.

NCBI # X85025 (SEQ ID NOs 264 and 265) relate to a human mRNA for a MN1-TEL fusion gene (type I). Nt 22..23 is said to be the fusion site.

15 del(5q)

Jaju et al., *Blood* 1999 Jul 15;94(2):773-80, reported a recurrent translocation, t(5;11)(q35;p15.5), associated with a del(5q) in childhood acute myeloid leukemia. Partial deletion of the long arm of chromosome 5, del(5q), is the cytogenetic hallmark of the 5q-syndrome, a distinct subtype of myelodysplastic syndrome-refractory anemia (MDS-RA). Deletions of 5q also occur in the full spectrum of other de novo and therapy-related MDS and acute myeloid leukemia (AML) types, most often in association with other chromosome abnormalities. However, the loss of genetic material from 5q is believed to be of primary importance in the pathogenesis of all del(5q) disorders.

Lindgren et al., *Am J Hum Genet* 1992 May;50(5):988-97, reported phenotypic, cytogenetic, and molecular studies of three patients with constitutional deletions of chromosome 5 in the region of the gene for familial adenomatous polyposis, APC, affiliated with colon cancer and polyps. High-resolution banding studies indicated that some deletions spans the region 5q21-q22..

Other potential deletion aberrations at the 5q locus include but are not limited to deletions at positions 5q13.3, corresponding to the RASA1 gene encoding the GAP RAS p21 protein activator 1 (GTPase activating protein), aberrancies of which are known to associate with basal cell carcinoma; 5q21, corresponding to the PST gene encoding PST1 Polysialyltransferase; 5q21-q22, corresponding to the APC gene, aberrancies of which correlate with colorectal cancer; 5q31, corresponding to the FACL6 gene encoding ACS2 Fatty-acid-Coenzyme A ligase, a long-chain 6 (long-chain acyl-CoA synthetase 2), aberrancies of which give rise to myelodysplastic syndrome and acute myelogenous leukemia; 5q31, encoding the GRAF GTPase regulator associated with the focal adhesion kinase, aberrancies of which give rise to juvenile myelomonocytic leukemia; 5q31.1, encoding IRF1, a MAR Interferon regulatory factor-1, aberrancies of which give rise to macrocytic anemiam myelodysplastic syndrome (preleukemic), acute myelogenous leukemia, gastric cancer, and nonsmall cell lung cancer; 5q33.2-q33.3, corresponding to CSF1R, FMS Colony-stimulating factor-1 receptor, aberranceis of which have been associated with oncogene FMS (McDonough feline sarcoma), and predisposition to myeloid malignancy; 5q35, encoding NPM1 Nucleophosmin 1 (nucleolar phosphoprotein B23, numatrin), aberrancies of which are known to associate with acute promyelocytic leukemia; 5q35.3, encoding gene FLT4, VEGFR3, encoding PCL fms-related tyrosine kinase-4 (vascular endothelial growth factor receptor, aberrancies of which contribute to hereditary lymphedema.

NCBI # NM_002387 (SEQ ID NOs 266 and 267) relate to a human gene that is found mutated in colorectal cancers(MCC) mRNA. Nt 221-2710 are said to represent coding sequence. Allelic variation is said to exist at nt 2869 (c/t).

del(7q)

Schwartz et al., Cytogenet. Cell Genet. 51: 152-153 (1991) reported deletion mapping of plasminogen activator inhibitor, type I (PLANH1) and beta-glucuronidase (GUSB) in 7q21-q22. Wedemeyer et al., Genomics 46: 313-315 (1997) reported the proximity of the human HIP1 gene close to the elastin (ELN) locus on 7q11.23. Dridi et al., Am. J. Med. Genet. 87: 134-138 (1999), reported skin elastic fibers in Williams syndrome and Dutly et al., Am. J. Med. Genet. 87: 134-138 (1999), reported unequal interchromosomal rearrangements corresponding to deletions in these genes, and affiliated

with Williams-Beuren syndrome. Naritomi et al., Hum. Genet. 80: 201-202 (1988), reported a microdeletion of the proximal long arm of chromosome 7 affiliated with Zellweger syndrome. Horiike et al., Leukemia. (1999) Aug;13(8):1235-42, reported distinct genetic involvement of the TP53 gene in therapy-related leukemia and myelodysplasia, with chromosomal 7 losses and their possible relationship to replication error phenotype and the development of therapy-related AML/MDS. Wong et al., Cancer Genet Cytogenet. 1995 Jul 1;82(1):70-2, reported biclonal acute monoblastic leukemia associated with del(7q). Particular sites of interest include 7q11.23, encoding PTPN12, PTPG1 Protein tyrosine phosphatase, nonreceptor-type, known to associate with colon cancer; 7q21-q22, encoding PEX1, ZWS1 Peroxisome biogenesis factor-1, associate with Zellweger syndrome-1, neonatal adrenoleukodystrophy and infantile Refsum disease; 7q22-q31.1, encoding SLC26A3, DRA, CLD Solute carrier family 26 (sulfate transporter), member 3, associated with colon cancer; 7q31-q32 SMOH, SMO Smoothed, Drosophila, homolog of 601500, associated with sporadic basal cell carcinoma.

del(20q)

A deletion in the long arm of chromosome 20 is a recurring abnormality in malignant myeloid disorders. Its occurrence suggests that the loss of genetic material on 20q provides a proliferative advantage to myeloid cells, possibly through the loss of a tumor-suppressor gene. Roulston et al., Blood 82: 3424-3429 (1993), examined a series of patients with the del(20q) using fluorescence in situ hybridization with unique sequence probes that map along the length of 20q and delineated a segment that is deleted in 95% of all patients they examined (18 of 19). In addition, they showed that the deletions are interstitial rather than terminal. The region of deletion extended from 20q11.2 to 20q12 and was flanked by RPN2 (180490) proximally and D20S17 distally. The SRC (190090) and ADA (102700) genes were found to be located within the commonly deleted segment.

Stoffel et al. (1996) generated a YAC contig map of 20q11.2-q13.1 in a region spanning about 18 Mb and representing about 40% of the physical length of 20q. The map contains the chromosomal regions deleted in MODY1 (125850) and in myeloid leukemia. Using this physical map, they refined the location of a myeloid tumor suppressor-related gene to an 18-cM interval (approximately 13 Mb) between RPN2 and D20S17.

Stoffel et al., Proc. Nat. Acad. Sci. 93: 3937-3941 (1996), correlated the occurrence of del(20q) in a broad spectrum of myeloid disorders, suggesting that the loss of genetic material on 20q could provide a proliferative advantage to myeloid cells, possibly through the loss of a tumor-suppressor gene. Stoffel et al. examined a series of patients with the del(20q) using fluorescence in situ hybridization (FISH) with unique sequence probes that map along the length of 20q, delineated a segment that is deleted in 95% of all patients examined (18 of 19), and showed that the deletions are interstitial rather than terminal. This region of deletion extends from 20q11.2 to q12, and is flanked by the RPN2 (proximal) and D20S17 loci (distal). The SRC and ADA genes are located within the commonly deleted segment.

t(11q23)

Shiah et al., Leukemia, (2002) 16(2):196-202, reported clinical and biological implications of partial tandem duplication of the MLL gene in acute myeloid leukemia without chromosomal abnormalities at 11q23. The clinical and biological features of acute myeloid leukemia (AML) with 11q23/MLL translocations are well known, but the characteristics of AML with partial tandem duplication of the MLL gene have not been explored comprehensively. Sheah et al analyzed MLL duplication in 81 AML patients without chromosomal abnormalities at 11q23, using Southern blotting, genomic DNA polymerase chain reaction (PCR), reverse-transcription PCR and complementary DNA sequencing. Nine patients showed partial tandem duplication of the MLL gene, including eight (12%) of the 68 with normal karyotype. Seven patients showed fusion of exon 6/exon 2 (e6/e2), one, combination of differentially spliced transcripts e7/e2 and e6/e2, and the remaining one, combination of e8/e2 and e7/e2. Among the patients with normal karyotype, children aged 1 to 15 showed a trend to higher frequency of MLL duplication than other patients (2/5 or 40% vs 6/62 or 10%, $P = 0.102$). The patients with tandem duplication of the MLL gene had a significantly higher incidence of CD11b expression on leukemic cells than did those without in the subgroup of patients with normal karyotype (75% vs 28%, $P = 0.017$). There were no significant differences in the expression of lymphoid antigens or other myeloid antigens between the two groups of patients. In adults, the patients with MLL duplication had a shorter median survival time than those without (4.5 months vs 12 months, $P = 0.036$). In conclusion, partial tandem duplication of the MLL gene is associated with increased expression of CD11b on leukemic blasts and

implicates poor prognosis in adult AML patients. The higher frequency of MLL duplication in children older than 1 year, than in other age groups, needs to be confirmed by further studies.

Ono et al., Cancer Res. 2002 Jan 15;62(2):333-7, reported that SEPTIN6, a human
5 homologue to mouse Septin6, is fused to MLL in infant acute myeloid leukemia with complex chromosomal abnormalities involving 11q23 and Xq24.

Borkhardt et al., Genes Chromosomes Cancer. 2001 Sep;32(1):82-8, reported an ins(X;11)(q24;q23) that fuses the MLL and the Septin 6/KIAA0128 gene in an infant with AML-M2.

10 Luo et al., Mol Cell Biol. 2001 Aug;21(16):5678-87, reported that ELL-associated factor 1 interaction domain is essential for MLL-ELL-induced leukemogenesis.

Kuwada et al., Cancer Res. 2001 Mar 15;61(6):2665-9, reported a t(11;14)(q23;q24) that generates an MLL-human gephyrin fusion gene along with a de facto truncated MLL in acute monoblastic leukemia.

15 Garcia-Cuellar et al., Oncogene. 2000 Mar 30;19(14):1744-51, reported that ENL, the MLL fusion partner in t(11;19), binds to the c-Abl interactor protein 1 (ABI1) that is fused to MLL in t(10;11)+.

Akao et al., Genes Chromosomes Cancer. 2000 Apr;27(4):412-7, reported an analysis of the rearranged genome and chimeric mRNAs caused by a t(6;11)(q27;q23)
20 chromosome translocation involving MLL in an infant acute monocytic leukemia.

Hayashi et al., Cancer Res. 2000 Feb 15;60(4):1139-45, reported a leukemic cell line, SN-1, associated with a t(11;16)(q23;p13).

So et al., Cancer Genet Cytogenet. 2000 Feb;117(1):24-7, analysed MLL-derived transcripts in an infant acute monocytic leukemia having a complex translocation
25 (1;11;4)(q21;q23;p16).

Kourlas et al., Proc Natl Acad Sci U S A. 2000 Feb 29;97(5):2145-50, identified a gene at 11q23 encoding a guanine nucleotide exchange factor that fuses with MLL in acute myeloid leukemia.

Taki et al., Proc Natl Acad Sci U S A. 1999 Dec 7;96(25):14535-40, reported that AF5q31, an AF4-related gene, is fused to MLL in infant acute lymphoblastic leukemia with an ins(5;11)(q31;q13q23).

Taki et al., Cancer Res. 1999 Sep 1;59(17):4261-5, reported that AF17q25, a putative septin family gene, fuses with the MLL gene in acute myeloid leukemia associated with a t(11;17)(q23;q25).

Busson-Le Coniat et al., Leukemia. 1999 Feb;13(2):302-6, reported MLL-AF1q fusion resulting from t(1;11) in an acute leukemia.

Slany et al., Mol Cell Biol. 1998 Jan;18(1):122-9, reported on the oncogenic capacity of HRX-ENL that requires the transcriptional transactivation activity of ENL and the DNA binding motifs of HRX.

Other articles of interest include, Super et al., Genes Chromosomes Cancer. 1997 Oct;20(2):185-95, *Identification of complex genomic breakpoint junctions in the t(9;11) MLL-AF9 fusion gene in acute leukemia*; Taki et al., Blood. 1997 Jun 1;89(11):3945-50, *The t(11;16)(q23;p13) translocation in myelodysplastic syndrome fuses the MLL gene to the CBP gene*; Taki Tet al., *Fusion of the MLL gene with two different genes, AF-6 and AF-5alpha, by a complex translocation involving chromosomes 5, 6, 8 and 11 in infant leukemia*, Oncogene. 1996 Nov 21;13(10):2121-30. Tanabe et al., *AF10 is split by MLL and HEAB, a human homolog to a putative Caenorhabditis elegans ATP/GTP-binding protein in an inv(10;11)(p12;q23q12)*, Blood. 1996 Nov 1;88(9):3535-45; Ma et al., *LAF-4 encodes a lymphoid nuclear protein with transactivation potential that is homologous to AF-4, the gene fused to MLL in t(4;11) leukemias*, Blood. 1996 Jan 15;87(2):734-45; Prasad et al., *Domains with transcriptional regulatory activity within the ALL1 and AF4 proteins involved in acute leukemia*, Proc Natl Acad Sci U S A. 1995 Dec 19;92(26):12160-4. Baffa et al., *Involvement of the ALL-1 gene in a solid tumor*, Proc Natl Acad Sci U S A. 1995 May 23;92(11):4922; Mitani, *Cloning of several species of MLL/MEN chimeric cDNAs in myeloid leukemia with t(11;19)(q23;p13.1) translocation*, Blood. 1995 Apr 15;85(8):2017-24; Tse et al., *A novel gene, AF1q, fused to MLL in t(1;11) (q21;q23), is specifically expressed in leukemic and immature hematopoietic cells*, Blood. 1995 Feb 1;85(3):650-6; Chen et al., *Acute promyelocytic leukemia: from clinic to molecular biology*, Stem Cells. 1995 Jan;13(1):22-31. Review; Rubnitz et al., *ENL, the*

- gene fused with HRX in t(11;19) leukemias, encodes a nuclear protein with transcriptional activation potential in lymphoid and myeloid cells, *Blood*. 1994 Sep 15;84(6):1747-52; Prasad et al., *Leucine-zipper dimerization motif encoded by the AF17 gene fused to ALL-1 (MLL) in acute leukemia*, *Proc Natl Acad Sci U S A*. 1994 Aug 16;91(17):8107-11;
- 5 Meerabux et al., *Molecular cloning of a novel 11q23 breakpoint associated with non-Hodgkin's lymphoma*, *Oncogene*. 1994 Mar;9(3):893-8; Gauwerky et al., *Chromosomal translocations in leukaemia*, *Semin Cancer Biol*. 1993 Dec;4(6):333-40. Review; Hunger et al., *HRX involvement in de novo and secondary leukemias with diverse chromosome 11q23 abnormalities*, *Blood*. 1993 Jun 15;81(12):3197-203; Morrissey et al., *A*
- 10 *serine/proline-rich protein is fused to HRX in t(4;11) acute leukemias*, *Blood*. 1993 Mar 1;81(5):1124-31; Tkachuk et al., *Involvement of a homolog of Drosophila trithorax by 11q23 chromosomal translocations in acute leukemias*, *Cell*. 1992 Nov 13;71(4):691-700.

t(5;12)(q31;p13)

- Yagasaki et al. described a fusion of LACS to a TEL/ETV6 gene in an acute
- 15 myeloblastic leukemia case having a t(5;12) chromosomal translocation. The human mRNA fusion sequence may be found in NCBI # AF102845 (SEQ ID NO 268). Nt 1-40 are said to derive from the TEL gene on chromosome 12 and nt 41-1172 are said to derive from the LACS gene on chromosome 5.

t(1;12)(q25;p13)

- Cazzaniga et al., *Blood* 94: 4370-4373 (1999), reported an instance of the tyrosine kinase Abl-related gene ARG fused to ETV6 in an AML-M4Eo patient having a
- t(1;12)(q25;p13) translocation, and cloned reciprocal chimeric transcripts associated with the event. The ETV6/TEL gene is rearranged in most patients with 12p13 translocations fused to a number of different partners. One of the chimeric proteins consisted of the
- 25 helix-loop-helix oligomerization domain of ETV6 and the SH2, SH3, and protein tyrosine kinase domains of ABL2. The reciprocal transcript ABL2-ETV6 was also detected in the patient's RNA by RT-PCR, although at a lower expression level.

t(12;15)(p13;q25)

Wai et al., *Oncogene*. 2000 Feb 17;19(7):906-15, reported an ETV6-NTRK3 gene fusion associated with such translocation.

5 Eguchi et al., *Blood*. 1999 Feb 15;93(4):1355-63, reported a similar fusion of ETV6 to neurotrophin-3 receptor TRKC in acute myeloid leukemia with t(12;15)(p13;q25).

Knezevich et al., *Nat Genet*. 1998 Feb;18(2):184-7; reported an ETV6-NTRK3 gene fusion in congenital fibrosarcoma.

10 NCBI # AF125808 (SEQ ID NOs 269 and 270) relate to a human ETS related protein-neurotrophic receptor tyrosine kinase fusion protein (ETV6-NTRK3 fusion) mRNA, partial cds. Nt 12-64 are said to derive from chromosome 12 and nt 65-980 from chromosome 15.

15 NCBI # AF041811 (SEQ ID NOs 271 and 272) relate to a human ETS related protein-growth factor receptor tyrosine kinase fusion proteins (ETV6-NTRK3 fusion) mRNA, partial cds. . Nt 1-336 are said to derive from chromosome 12 and nt 337-1403 from chromosome 15.

t(1;12)(q21;p13)

Salomon-Nguyen et al., *Proc Natl Acad Sci U S A*. (2000) 97(12):6757-62, reported a t(1;12)(q21;p13) translocation observed in a case of acute myeloblastic
20 leukemia (AML-M2). At the protein level, the untranslocated TEL copy and, as a result of the t(1;12) translocation, a fusion protein containing the amino-terminal part of TEL and essentially all of the ARNT gene (126110), were expressed. The TEL/ETV6 gene is located at 12p13 and encodes a member of the ETS family of transcription factors. Translocated ETS leukemia (TEL) is frequently involved in chromosomal translocations
25 in human malignancies, usually resulting in the expression of fusion proteins between the amino-terminal part of TEL and either unrelated transcription factors or protein tyrosine kinases. ARNT (aryl hydrocarbon receptor nuclear translocator) belongs to a subfamily of the "basic region helix-loop-helix" (bHLH) protein that shares an additional region of similarity called the PAS (Per, ARNT, SIM) domain. ARNT is the central partner of

several heterodimeric transcription factors, including those containing the aryl hydrocarbon (dioxin) receptor (AhR) and the hypoxia-inducible factor 1 alpha (HIF1alpha). Interference with the activity of AhR or HIF1alpha may contribute to leukemogenesis.

2. Mutant Protein or Cellular Protein Isoforms

The second group of target proteins are mutants or isoforms (*e.g.* splice variants) of normal cellular proteins (usually the products of tumor suppressor genes) that, due to their mutant nature, exhibit a heightened dependence on HSP90 chaperone functions or else increased sensitivity, *i.e.*, instability, due to HSP90 inhibitors. The mutant or isoform proteins either (a) have become overtly oncogenic (a “dominant-positive” (DP) effect), or (b) exert a “dominant-negative” (DN) effect on their normal counterpart, thus preventing the normal protein’s tumor suppressor activity, and resulting in a net oncogenic effect. The examples are largely illustrated with respect to human sequences, although the person of ordinary skill will appreciate that homologs in other organisms are likewise included within the purview of the invention.

a. v-src

One such example of a mutant or isoform protein is human v-src (NCBI #s NM_005417; SEQ ID NOs 273 and 274), which counterpart, c-src (NCBI # XM_044659 (SEQ ID NOs 275 and 276), corresponds to the normal cellular gene product. As described above, proteins with a heightened dependence on HSP90 can be identified by their enhanced sensitivity to degradation induced by HSP90 inhibitors, such as the ansamycin antibiotic geldanamycin. Ansamycins and other HSP90 inhibitors were originally isolated on the basis of their ability to revert v-src transformed fibroblasts (Uehara, Y. *et al.*, 1985, *Supra*, 76: 672-675) and this reversal was correlated with the functional inactivation of the v-src protein (Uehara, Y. *et al.*, 1986, *Mol. Cell. Biol.*, 6: 2198-2206). This effect was subsequently reported to be caused by the ubiquitin/proteasome-dependent degradation of the transforming v-src protein as a result of inhibition of HSP90 function by geldanamycin (Whitesell, L., *et al.*, 1994, *supra*). Finally, a recent study compared the rate and potency of degradation of v-src and c-src proteins after treatment of Rous sarcoma virus-transformed 3T3 fibroblasts with the ansamycin geldanamycin. In this study, the oncogenic mutant v-src protein was almost 100% degraded within 6 hours (An, W *et al.*, 2000, *supra*, see Figure 2), whereas the normal cellular counterpart, c-src, was largely unaffected even after 20 hours of the same treatment (An, W *et al.*, 2000, *supra*, see Figure 4).

HSP90 inhibitors can selectively induce degradation of a wide range of mutated or otherwise aberrant proteins that cause or exacerbate a disease, and that have an apparent heightened dependence on HSP90.

b. RET

5 An example of a dominant proto-oncogene encoding a signaling protein that is mutated in certain human cancers giving rise to constitutively active structurally abnormal cellular proteins is the *RET* proto-oncogene (NCBI # P07949; SEQ ID NO 277) in multiple endocrine neoplasia Type 2 (MEN-2). *RET* encodes a receptor tyrosine kinase whose ligand is presently unidentified (Kolibaba, K, *et al*, 1997, *Supra*). The germline mutations found in MEN-2A patients (Cys634→
10 Arg/Tyr, similar mutations at Cys609, 611, 618 and 620) alter the tertiary structure of the protein resulting in homodimerization and activation of the kinase domain. The commonly observed mutation in MEN-2B, Met918→Thr, alters the kinase domain structure, causing activation directly. Both of these pathways involve alterations in protein conformation, which again implicates HSP90 and underscores the broad utility of the invention.

c. p53

15 Another example of a mutant, oncogenic variant group of a normal cellular protein is tumor suppressor antigen p53. The wild-type protein and mRNA sequences for p53 are found in NCBI accession # M14695 (SEQ ID NOs 278 and 279). However, numerous mutations in p53 are known to occur and represent the most common molecular genetic defects found in human
20 cancers (Harris, C *et al*, 1993, *N. Engl. J. Med.* 329:1318-1327). A mutant p53 protein was reportedly degraded in cells following treatment with geldanamycin, but wild type p53 exhibited no such, or only minimal, degradation (Blagosklonny, M *et al*, 1995, *Oncogene*, 11:933-939). Unlike the situation described above for v-src, most p53 mutations are “loss of function” effects , *i.e.*, the mutation results in the inability of the protein to perform one or more of its normal
25 functions. Thus, in a tumor cell that has an intact p53 allele and a loss of function mutant allele, simply causing the mutant form to be degraded will not change cellular behavior. However, if the mutant protein by some mechanism inhibits the action of its coexpressed normal counterpart inside tumor cells, then degrading it will affect cellular behaviour.

This “dominant-negative” (DN) effect has been shown to occur in cells harboring certain
30 p53 mutants, and by several different mechanisms. For example, a mutant may afford tighter

DNA binding without transactivation (Chene, P, *et al*, 1999, *Int. J. Cancer*. 82:17-22). This type of p53 mutant does not exhibit “classical” DN activity unless the mutation confers an increased affinity for DNA, because the mutant stoichiometrically competes with the wild type (WT) protein for binding to DNA. Another example is inhibition of tetramerization by incorporation of one or more mutant p53s into a complex with WT proteins (Deb, D *et al*, 1999, *Int. J. Oncol.* 15:413-422, Rollenhagen, C *et al*, 1998, *Int. J. Cancer* 78:372-376). Yet a third example concerns “prion-like” activity, in which a mutant protein forces a WT protein into a mutant conformation that then impairs its ability to bind to DNA and/or transactivate p53 target genes (Chene, P, 1998, *J. Mol. Biol.* 281:205-209)

Increased stability of mutants relative to WT proteins causes them to accumulate and override normal p53 biology. This is counterintuitive given the fact that p53 has a built-in negative feedback loop on its own transcription (via induction of the mdm-2 protein, which subsequently targets p53 for degradation). If the increased stability of a given mutant were due solely to failure to transactivate mdm-2, then accumulation of the mutant would not occur in the presence of a WT allele (Blagosklonny, M, 2000, *FASEB J.* 14:1901-1907) because this protein would initiate negative feedback mechanisms that would be expected to act on both WT and mutant p53.

On the other hand, an independent mechanism favoring mutant accumulation (*e.g.* protection by association with HSP90 (Smith, D, *et al*, 1998, *supra*; Sepehrnia, B, *et al*, 1996, *J. Biol. Chem.* 271:15084-15090) would permit a “recessive” mutant to become in sufficient excess of the transactivating form to result in progressive inhibition of the negative feedback pathways. In this situation, the mutant would have a net DN effect due to progressive accumulation of a stoichiometric antagonist, and selective degradation of that mutant by inhibition of HSP90 activity would be expected to restore normal p53 function. Thus, in most or all cases, a DN phenotype produced by mutant p53 is secondary to the activity of HSP90 and inhibition of HSP90 function with 17-AAG or other HSP90 ATP binding site antagonists would prevent the expression of the DN phenotype and so rescue normal p53 function.

i. Dominant negative p53 mutants

A list of exemplary p53 mutations, including examples of structurally-abnormal proteins, dominant-negative proteins, prion-like proteins, and mutants with various combinations of these properties, follows:

Chene *et al*, 1999, *Int. J. Cancer*. 82:17-22; Y236delta (deletion of codon 236) resulted in a conformationally altered & dominant-negative phenotype.

Preuss *et al*, 2000, *Int. J. Cancer* 88:162-171); C174Y (Cys→Tyr) (rat) is dominant-negative, non-transactivating. The same mutation at position 176 is predicted to have a similar effect in humans, as the respective homologs have close correlative structural similarities at these positions.

Srivastava *et al*, 1993, *Oncogene* 8:2449-2456); M133T (Met→Thr), G245D (Gly→Asp), and E258K (Glu→Lys) all display conformationally altered, dominant-negative, prion-like displaying activity, in that co-incubation with WT p53 converts it into the mutated conformation.

Deb *et al*, 1999, *Int. J. Oncol.* 15:413-422); 1-293delta (deletion of codons 1-293) exhibited dominant negative DNA binding characteristics without transactivating activity.

Frebourg *et al*, 1992, *Proc. Natl. Acad. Sci.* 89:6413-6417; G245C (Gly→Cys), R248W (Arg→Trp), E258K (Glu→Lys), and R282W (Arg→Try) all independently display conformationally altered, dominant-negative activity.

Brachmann *et al*, 1996, *Proc. Natl. Acad. Sci.* 93:4091-4095; novel yeast assay used to identify dominant-negative p53 mutants that have also been found in human tumors, specifically implicating codons 132, 135, 151, 158, 176, 179, 236, 241, 242, 244, 245, 246, 248, 257, 265, 273, 277, 278, 279, 280, and 281. Of particular interest because they exhibited the greatest dominant-negative activity were mutants at codons 241, 242, 244, 245, 246, 248, 277, 278, 279, 280, and 281.

Blagosklonny *et al*, 1995, *Oncogene* 11:933-939); p53s mutated at the following codons exhibited disrupted conformations were dominant negative, and sensitive to geldanamycin: R175H (Arg→His), 194, 213, 223, 248, 274, R280K (Arg→Lys).

Aurelio *et al*, 2000, *Mol. Cell. Biol.* 20:770-778; without identifying conformational status, the following mutants were identified as dominant-negative for transactivation of apoptotic signals (Bax), but not growth arrest signals (p21^{WAF}): V143A (Val→Ala), R175H (Arg→His), G245C (Gly→Cys), R248W (Arg→Trp), R273H (Arg→His), K305M (Lys→Met), G325V (Gly→Val).

Marutani *et al*, 1999, *Cancer Res.* 59:4765-4769; yeast-based transdominance assay used to identify dominant-negative mutations at 16 codons : R156H (Arg→His), R175H (Arg→His), P177S (Pro→Ser), H178P (His→Pro), H179R (His→Arg), R181P (Arg→Pro), 238-9delta (deletion of codons 238 & 239), G245S (Gly→Ser), G245D (Gly→Asp), M246R (Met→Arg),
 5 R248Q (Arg→Gln), R249S (Arg→Ser), R273H (Arg→His), R273C (Arg→Cys), R273L (Arg→Leu), D281Y (Asp→Tyr).

ii. Dominant positive p53 mutants

In addition to dominant-negative mutations, some p53 mutations actually transactivate inappropriate gene expression, contributing to oncogenesis; *i.e.* a positive tumor promoting effect.
 10 See Park *et al*, 1994, *Oncogene* 9:1899-1906. This type of mutation is particularly suited to the approach embodied in the present invention because, unlike in the dominant-negative situation, the presence or absence of a normal allele of the tumor suppressor gene is irrelevant to the therapeutic utility of the HSP90 inhibitor. In other words, because the mutant p53 itself contributes to the malignant process, destruction of the mutant protein by inhibition of HSP90 is
 15 expected to have direct therapeutic value. A good example is C176Y (Cys→Tyr), as reported by Preuss, U *et al*, 2000, *Int. J. Cancer* 88:162-171. This mutant induces rather than represses the cellular fos promoter, resulting in activation of oncogenic signaling pathways. The biology of “dominant-positive” p53 mutants is reviewed in van Oijen *et al*, 2000, *Clin. Cancer Res.* 6:2138-2145. Other examples of mutations of p53 that give rise to tumorigenic phenotypes include, but
 20 are not limited to, Phe-132, Val-135, Ala-143, His-175, His-179, Trp-248, Ser-249, Leu-273, His-273 and Gly-281. Of particular interest, because these mutant proteins have been shown to be disrupted conformationally, are Ala-143, His-175, His-179 and Gly-281 (van Oijen, M, *et al*, 2000, *supra*). Particular subsets of the above list of tumor-promoting mutants have been shown to exert their oncogenic effects via transactivation of one or more of the growth promoting genes
 25 *bFGF*, *IGF-1*, *EGF-R*, and *c-myc*. Alternatively or conjunctively, some gain-of-function mutants, including Ala-143, His-175, Trp-248, Ser-249, His-273, and Gly-281, contribute to tumor resistance to chemotherapeutic drugs by transactivating the *MDR* gene.

As described above, in the case of this type of mutant, in heterozygous cells, selective degradation of that mutant by inhibition of HSP90 activity will restore normal p53 function.
 30 Furthermore, in cases of loss of heterozygosity (LOH), where the tumor has progressed further and the second, normal p53 allele has become mutated or lost, selective degradation of the

mutated protein by inhibition of HSP90 chaperoning will result in a therapeutic effect. In this case the p53 mutant is behaving as an oncoprotein, as in the bcr-abl and v-src examples described above.

d. Other tumor suppressor variant proteins

5 In addition to p53 itself, additional members of the p53 family of tumor suppressor proteins have also been implicated in human cancer progression. Although p53 itself is a fairly ubiquitous protein, other family members have more restricted tissue distributions. In particular tissues and tumors derived therefrom, closely related non-p53 proteins serve the same role as p53 itself. In these tumors, a truncated variant, termed deltaN,
10 predominates over the full-length form. The truncated and/or deletent isoform is able to compete with the full length form for DNA binding, but does not itself have any transactivating activity. Thus, the deltaN form inhibits the tumor suppressor activity of the full length form, so that if the variant is degraded as a result of inhibition of HSP90 activity, an antitumor effect or drug-sensitizing effect will result. The deltaN isoform will
15 have a heightened dependence on HSP90.

The following three examples concern the specific tumor suppressor proteins p51, p63, and p73. p51 and p63 are each produced from a common 15 exon gene, p73L/p63/p51/p40/KET, and all three proteins exhibit various isoforms, including deltaN isoforms that lack N-terminal transactivation (TA) domains and which are implicated in
20 various carcinomas treatable according to methods of the invention. The many isotypes possible for these gene products are attributable, at least in part, to complex alternative splicing events and, in the case of p63, multiple promoters. For each, it is understood that isoforms may exist and specific isoform expression patterns may vary as between different tissue types, and as between normal versus carcinomic or neoplastic tissues.

25 i. deltaN p51

Osada et al. described the cloning and functional analysis of human p51, which structurally and functionally resembles p53. Nature Med. 4: 839-843 (1998). Two major splicing variant gene products have been detected in normal cells, p51A and p51B. p51A (aka TAp63gamma; NCBI #s AB016072 (SEQ ID NOs 280 and 281) is a 448-amino-acid protein with
30 a molecular weight of 50.9 kDa; and p51B (aka TAp63alpha; AB016073 (SEQ ID NOs 282 and

283) is a 641-amino-acid protein with a molecular weight of 71.9 kDa. Other encoded isoforms have also been observed, including, e.g., those denoted in the following list: p51 delta (NCBI # AF116771 (SEQ ID NOs 284 and 285), delNdelta (NCBI # AAF43493 (SEQ ID NOs 286 and 287), delNbeta (NCBI # AAF43492 (SEQ ID NOs. 288 and 289), delNalpha (NCBI # AAF43491 (SEQ ID NOs. 290 and 291), delNgamma (NCBI # AAF43490; SEQ ID NOs 292 and 293), TAp63delta (NCBI # AAF43489; SEQ ID NOs 294 and 295), TAp63beta (NCBI # AAF43488 (SEQ ID NOs 296 and 297), TAp63alpha (NCBI # AAF43487 (SEQ ID NOs 298 and 299), and TAp63gamma (NCBI # AAF43486 (SEQ ID NOs 300 and 301). The TA isoforms contain a transactivation domain (encoded by exon 3') for transactivating p53; the deltaN forms do not. The absence of the TA domain is thought to render those particular isoforms nonfunctional, thereby contributing to carcinoma etiology at least when those isoforms are expressed in abnormally high amounts. Normal expression patterns of the various isotypes is known to vary as between different tissue types. In lung cancer specimens, for example, multiple deltaN ("TA-less") forms of the p51 protein were found to be overexpressed in 34 of 44 lung cancer specimens analysed (77%). (Tani, M *et al*, 1999, *Neoplasia* 1:71-79).

ii. deltaN p63

In certain bladder and nasopharyngeal carcinomas, various isoforms of the p53 family member p63 are expressed, and one or more of the deltaN forms, e.g., deltaN p63beta (NCBI # AF075433; SEQ ID NOs 302 and 303), deltaN p63gamma (NCBI # AF075429; SEQ ID NOs 304 and 305), and deltaN p63 alpha (NCBI # AF075431 (SEQ ID NOs 306 and 307) predominate and dominantly inhibit the transactivating activity of the full length TA-containing forms. (Park, B *et al*, 2000, *Cancer Res.* 60:3370-3374). The TA-containing isoforms are TA p63 beta (NCBI # AF075432; SEQ ID NOs 308 and 309) and TA p63 alpha (NCBI # AF075430; SEQ ID NOs 310 and 311). In nasopharyngeal carcinoma, the deltaN isoform predominance is even more pronounced (Crook, T *et al*, 2000, *Oncogene* 19:3439-3444). The p63 protein is also important in UV-B-induced skin cancer. Overexpression of the deltaN isoform of p63 in transgenic mouse epidermis was found to block apoptosis induced by WT p53 in response to UV-B irradiation (Liefer, K, *et al*, 2000, *Cancer Res.* 60:4016-4020). Mutations in the *p63* gene have also been reported in epidermal carcinomas. See, e.g., Osada *et al*, 1998, *Nat. Med.* 4:839-843 and NCBI # NM003722 (SEQ ID NOs 312 and 313).

iii. deltaN p73

The p73 protein is important in ovarian carcinoma – when compared to primary cultures of normal ovarian epithelial cells, 57% of ovarian carcinoma cell lines, 71% of invasive tumors and 92% of borderline tumor tissues were found to express elevated levels of deltaN p73 (Ng, S *et al*, 2000, *Oncogene* 19:1885-1890). Full-length p73 and isoforms thereof are displayed in NCBI # Y11416 (SEQ ID NOs 314, 315, 316, and 317), along with splice and allelic variations, including splice variations responsible for the deltaN isoform.

Applicants expect that all of the foregoing truncated p53 family members are structurally unstable, dependent on HSP90 and/or exhibit increased sensitivity to HSP90 inhibitors relative to their wild-type counterparts. Applicants further anticipate that other isomeric/aberrant forms of proteins may exhibit similar behavior(s).

The methods of the present invention may be used on mammals, preferably humans, either alone or in combination with other therapies or methods useful for treating a particular cell proliferative disorder or viral infection.

The use of the present invention is facilitated by first identifying whether the cell proliferation disorder or viral infection is accompanied by cells which contain expression of a fusion oncoprotein or a mutated cellular protein with heightened dependence on HSP90 (or a fusion protein or mutant protein that, by one skilled in the art, would be predicted to have heightened dependence on HSP90). Once such disorders are identified, patients suffering from such a disorder can be identified by analysis of their symptoms by procedures well known to medical doctors. Such patients are treated as described herein.

3. Representative assays for diagnosing proliferative disorders

Many different types of methods are known in the art that can be used to diagnose a proliferative disorder characterized by an aberrant protein, *e.g.*, those that involve determining protein concentrations and measuring or predicting the level of proteins within cells, tissues, and fluid samples. Indirect techniques include nucleic acid hybridization and amplification using, *e.g.*, polymerase chain reaction (PCR). These techniques are known to the person of skill and are discussed, *e.g.*, in Sambrook, Fritsch & Maniatis, *Molecular Cloning: A Laboratory Manual*, Second Edition (1989) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., Ausubel, *et al.*, *Current Protocols in Molecular Biology*, John Wiley & Sons, NY, 1994. Because the nucleic acid sequence is

known, and because the aberrant proteins have a foundational basis in the nucleic acid sequence, the specific sequences found for aberrant proteins can also be used to generate primers and probes that span the novel junction (in the case of fusion proteins), *e.g.*, using RT-PCR and other procedures. For non-fusion proteins, as well as fusion proteins,
5 stringent hybridization and/or PCR can be used diagnostically.

Polyclonal or monoclonal antibodies can also be generated based on the specific sequence of the aberrant protein (in the case of fusion proteins, preferably the novel amino acid junction itself) using routine techniques. See Harlow *et al.*, *Antibodies: A Laboratory Manual*, 2nd Ed; Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1988).

10 Examples of diagnostic methods of that can be used with the invention include those reviewed in Slominski, A *et al*, 1999, *Arch. Pathol. Lab. Med.* 123:1246-1259, O'Connor *et al*, 1999, *Leuk. Lymphoma* 33:53-63, and Scarpa, A *et al*, 1997, *Leuk. Lymphoma* 26 Suppl. 1:77-82. A further list of methods that is intended to be exemplary but not to limit the scope of the invention, follows.

15 O'Connor *et al* , 1997, *Br. J. Haematol.* 99:597-604 described that the t(15;17)(q22;q21) translocation found in APL produces a PML-RAR fusion protein that can be specifically detected with the 5E10 Mab by fluorescence activated cell sorting (FACS).

Le *et al* , 1998, *Eur. J. Haematol.* 60:217-225 reported that the AML-ETO fusion protein that arises in t(8;21) AML can be identified in tumor cells with ETO-specific polyclonal
20 antibodies using western blotting. The normal ETO protein (70kD) can be distinguished from the AML-ETO fusion protein (94kD) on the basis of their differing mobilities in the gel.

Viswanatha *et al* , 1998, *Blood* 91:1882-1890 found that the CBFβ-SMMHC fusion protein present in Inv(16)(p13q32) and t(16;16)(p13;q32) AML can be specifically detected with a polyclonal antibody specific for a junctional epitope using FACS of permeabilized cells.

25 In the case of dominantly-acting mutant proteins, such as mutant RET or gain-of-function mutants of p53, the presence of the specific point mutations known to give rise to the dominant mutant may be identified by the molecular genetic techniques listed above in reference to fusion proteins. Numerous reviews of germline and acquired p53 mutations detected in human cancers have been published (*see, e.g.*, Hainuit, P, *et al*, 2000, *Adv. Cancer Res.* 77:81-137).

In the case of dominant-negative p53 mutations, several other diagnostic criteria may be employed to identify patients susceptible of treatment with the current invention. First, molecular genetic methodologies such as Southern Blotting or PCR can be used to detect the presence of a specific point mutation known to give rise to a dominant-negative version of p53. Similarly, FISH
5 may be employed to detect specific point mutations known to confer conformational changes and/or dominant-negative activity (Villadsen R *et al*, 2000, *Cancer Genet. Cytogenet.* 116:28-34). Other methods include allele-specific PCR (AS-PCR) and chromosome flow cytometry (Villadsen *et al*, *Supra*).

Alternatively, if the mutation in question has not previously been shown to generate a
10 dominant-negative p53 mutant, a cell-based transdominance assay may be used to determine the phenotype (Frebourg, T *et al*, 1992, *Proc. Natl. Acad. Sci.* 89:6413-6417). In this assay, p53-null SAOS-2 cells are co-transfected with WT p53 and the test mutant. The normal p53 protein causes the cells to undergo apoptosis, from which fate they can be rescued by a p53 mutant that has a dominant negative activity. In these cases, further genetic analyses may be performed to confirm
15 the presence of an intact non-mutant allele. In addition, antibodies have been raised that distinguish between p53 proteins with normal versus mutant conformation. These latter p53s have a heightened dependence upon HSP90, and so fall within the scope of the present invention. Specifically, PAb240, from (Oncogene Sciences, Inc.) OSI, is mutant conformation-specific. The corresponding antibody specific for WT is PAb1620, also for OSI (Chene, P, *et al*, 1999, *supra*).

In the case of cell proliferative disorders arising due to unwanted proliferation of non-cancer cells, the level of the fusion protein or mutated cellular protein is compared to that level occurring in the general population (*e.g.*, the average level occurring in the general population of people or animals excluding those people or animals suffering from a cell proliferative disorder). If the unwanted cell proliferation disorder is characterized by an abnormal level of a fusion
20 protein than occurs in a normal population, or by the presence of a mutated cellular protein, such as p53, then the disorder is a candidate for treatment using the methods described herein. In a preferred example, the mutated protein is p53 and the proliferative disorder is rheumatoid arthritis. In a particularly preferred example, the p53 mutations may include, but are not limited to, N239S (Asn→Ser), C176R (Cys-Arg) and R213* (Arg→stop) and the mutant forms exert
25 apparent dominant-negative activity over the wild-type protein. (Han, Z *et al*, 1999, *Arthritis Rheum.* 42:1088-1092).
30

4. Preparation and Administration of Pharmaceutical Compositions

Geldanamycin may be prepared according to U.S. Patent No. 3,595,955 using the subculture of *Streptomyces hygroscopicus* that is on deposit with the U.S. Department of Agriculture, Northern Utilization and Research Division, Agricultural Research, Peoria, Ill., USA, accession number NRRL 3602. It is also available from Sigma/Aldrich Chemical Co., St. Louis, Mo., USA. Numerous derivatives of this compound, including herbimycin A, macbecin, and 17-AAG may be fashioned as specified in U.S. Patent Nos. 4, 261, 989, 5,387,584, and 5,932,566, or according to standard techniques known in the art. Other useful ansamycin derivatives appear in Applicants' co-pending and commonly owned provisional application entitled, "*Ansamycins Having Improved Pharmacological and Biological Properties*," filed February 8, 2002, Serial Number to be determined, and herein incorporated by reference in its entirety.

Those of ordinary skill in the art are familiar with formulation and administration techniques that can be employed in use of the invention, *e.g.*, as discussed in Goodman and Gilman's *The Pharmacological Basis of Therapeutics*, current edition; Pergamon Press; and Remington's *Pharmaceutical Sciences* (current edition.) Mack Publishing Co., Easton, Pa.

The compounds utilized in the methods of the instant invention may be administered either alone or in combination with pharmaceutically acceptable carriers, excipients or diluents, in a pharmaceutical composition, according to standard pharmaceutical practice. The compounds can be administered orally or parenterally, including the intravenous, intramuscular, intraperitoneal, subcutaneous, rectal and topical routes of administration.

The pharmaceutical compositions used in the methods of the instant invention can contain the active ingredient in a form suitable for oral use, for example, as tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, hard or soft capsules, or syrups or elixirs. Compositions intended for oral use may be prepared according to any method known to the art for the manufacture of pharmaceutical compositions and such compositions may contain one or more agents selected from the group consisting of sweetening agents, flavoring agents, coloring agents and preserving agents in order to provide pharmaceutically elegant and palatable preparations. Tablets contain the active ingredient in admixture with non-toxic pharmaceutically acceptable excipients which are suitable for the manufacture of tablets. These excipients may be, for example, inert diluents, such as calcium carbonate, sodium carbonate,

lactose, calcium phosphate or sodium phosphate; granulating and disintegrating agents, such as microcrystalline cellulose, sodium crosscarmellose, corn starch, or alginic acid; binding agents, for example starch, gelatin, polyvinyl-pyrrolidone or acacia, and lubricating agents, for example, magnesium stearate, stearic acid or talc. The tablets may be uncoated or they may be coated by known techniques to mask the unpleasant taste of the drug or delay disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a water soluble taste masking material such as hydroxypropylmethyl-cellulose or hydroxypropylcellulose, or a time delay material such as ethyl cellulose, cellulose acetate butyrate may be employed.

Formulations for oral use may also be presented as hard gelatin capsules wherein the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with water soluble carrier such as polyethyleneglycol or an oil medium, for example peanut oil, liquid paraffin, or olive oil.

Aqueous suspensions contain the active material in admixture with excipients suitable for the manufacture of aqueous suspensions. Such excipients are suspending agents, for example sodium carboxymethylcellulose, methylcellulose, hydroxypropylmethyl-cellulose, sodium alginate, polyvinyl-pyrrolidone, gum tragacanth and gum acacia; dispersing or wetting agents may be a naturally-occurring phosphatide, for example lecithin, or condensation products of an alkylene oxide with fatty acids, for example polyoxyethylene stearate, or condensation products of ethylene oxide with long chain aliphatic alcohols, for example heptadecaethylene-oxycetanol, or condensation products of ethylene oxide with partial esters derived from fatty acids and a hexitol such as polyoxyethylene sorbitol monooleate, or condensation products of ethylene oxide with partial esters derived from fatty acids and hexitol anhydrides, for example polyethylene sorbitan monooleate. The aqueous suspensions may also contain one or more preservatives, for example ethyl, or n-propyl p-hydroxybenzoate, one or more coloring agents, one or more flavoring agents, and one or more sweetening agents, such as sucrose, saccharin or aspartame.

Oily suspensions may be formulated by suspending the active ingredient in a vegetable oil, for example arachis oil, olive oil, sesame oil or coconut oil, or in mineral oil such as liquid paraffin. The oily suspensions may contain a thickening agent, for example beeswax, hard paraffin or cetyl alcohol. Sweetening agents such as those set forth above, and flavoring agents

may be added to provide a palatable oral preparation. These compositions may be preserved by the addition of an anti-oxidant such as butylated hydroxyanisol or alpha-tocopherol.

Dispersible powders and granules suitable for preparation of an aqueous suspension by the addition of water provide the active ingredient in admixture with a dispersing or wetting agent, suspending agent and one or more preservatives. Suitable dispersing or wetting agents and suspending agents are exemplified by those already mentioned above. Additional excipients, for example sweetening, flavoring and coloring agents, may also be present. These compositions may be preserved by the addition of an anti-oxidant such as ascorbic acid.

The pharmaceutical compositions used in the methods of the instant invention may also be in the form of oil-in-water emulsions. The oily phase may be a vegetable oil, for example olive oil or arachis oil, or a mineral oil, for example liquid paraffin or mixtures of these. Suitable emulsifying agents may be naturally-occurring phosphatides, for example soy bean lecithin, and esters or partial esters derived from fatty acids and hexitol anhydrides, for example sorbitan monooleate, and condensation products of the said partial esters with ethylene oxide, for example polyoxyethylene sorbitan monooleate. The emulsions may also contain sweetening, flavoring agents, preservatives and antioxidants.

Syrups and elixirs may be formulated with sweetening agents, for example glycerol, propylene glycol, sorbitol or sucrose. Such formulations may also contain a demulcent, a preservative, flavoring and coloring agents and antioxidant.

The pharmaceutical compositions may be in the form of sterile injectable aqueous solutions. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution and isotonic sodium chloride solution.

The sterile injectable preparation may also be a sterile injectable oil-in-water microemulsion where the active ingredient is dissolved in the oily phase. For example, the active ingredient may be first dissolved in a mixture of soybean oil and lecithin. The oil solution then introduced into a water and glycerol mixture and processed to form a microemulsion.

The injectable solutions or microemulsions may be introduced into a patient's blood-stream by local bolus injection. Alternatively, it may be advantageous to administer the solution or microemulsion in such a way as to maintain a constant circulating concentration of the instant

compound. In order to maintain such a constant concentration, a continuous intravenous delivery device may be utilized. An example of such a device is the Deltec CADD-PLUS™ model 5400 intravenous pump.

The pharmaceutical compositions may be in the form of a sterile injectable aqueous or oleagenous suspension for intramuscular and subcutaneous administration. This suspension may be formulated according to the known art using those suitable dispersing or wetting agents and suspending agents which have been mentioned above. The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally-acceptable diluent or solvent, for example as a solution in 1,3-butane diol. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

The HSP90 inhibitors used in the methods of the present invention may also be administered in the form of a suppositories for rectal administration of the drug. These compositions can be prepared by mixing the inhibitors with a suitable non-irritating excipient which is solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum to release the drug. Such materials include cocoa butter, glycerinated gelatin, hydrogenated vegetable oils, mixtures of polyethylene glycols of various molecular weights and fatty acid esters of polyethylene glycol.

For topical use, creams, ointments, jellies, solutions or suspensions, etc., containing an HSP90 inhibitor can be used. (As used herein, topical application can include mouth washes and gargles.)

The compounds used in the methods of the present invention can be administered in intranasal form via topical use of suitable intranasal vehicles and delivery devices, or via transdermal routes, using those forms of transdermal skin patches well known to those of ordinary skill in the art. To be administered in the form of a transdermal delivery system, the dosage administration will, of course, be continuous rather than intermittent throughout the dosage regimen.

The HSP90 inhibitors used in the instant invention may also be co-administered with other well known therapeutic agents that are selected for their particular usefulness against the

condition that is being treated. For example, the instant compounds may be useful in combination with known anti-cancer and cytotoxic agents. The instant compounds may also be useful in combination with other inhibitors of parts of the signaling pathway that links cell surface growth factor receptors to nuclear signals initiating cellular proliferation.

5 The methods of the present invention may also be useful with other agents that inhibit angiogenesis and thereby inhibit the growth and invasiveness of tumor cells, including, but not limited to VEGF receptor inhibitors, angiostatin and endostatin.

 When a HSP90 inhibitor used in the methods of the present invention is administered into a human subject, the daily dosage will normally be determined by the prescribing physician with
10 the dosage generally varying according to the age, weight, and response of the individual patient, as well as the severity of the patient's symptoms.

 In one exemplary application, a suitable amount of a HSP90 inhibitor is administered to a mammal undergoing treatment for cancer. Administration occurs in an amount of each type of inhibitor of between about 0.1 mg/kg of body weight to about 60 mg/kg of body weight per day,
15 preferably of between 0.5 mg/kg of body weight to about 40 mg/kg of body weight per day. A particular therapeutic dosage that comprises the instant composition includes from about 0.01 mg to about 1000 mg of a HSP90 inhibitor. Preferably, the dosage comprises from about 1 mg to about 1000 mg of a HSP90 inhibitor.

 Examples of antineoplastic agents which can be used in combination with the methods of
20 the present invention include, in general, alkylating agents, anti-metabolites; epidophyllotoxin; an antineoplastic enzyme; a topoisomerase inhibitor; procarbazine; mitoxantrone; platinum coordination complexes; biological response modifiers and growth inhibitors; hormonal/anti-hormonal therapeutic agents and haematopoietic growth factors.

 Exemplary classes of antineoplastic agents further include the anthracycline family of
25 drugs, the vinca drugs, the mitomycins, the bleomycins, the cytotoxic nucleosides, the epothilones, discodermolide, the pteridine family of drugs, diynenes and the podophyllotoxins. Particularly useful members of those classes include, for example, carminomycin, daunorubicin, aminopterin, methotrexate, methopterin, dichloromethotrexate, mitomycin C, porfiromycin, 5-fluorouracil, 6-mercaptopurine, gemcitabine, cytosine arabinoside, podophyllotoxin or podophyllotoxin derivatives such as etoposide, etoposide phosphate or teniposide, melphalan,
30

vinblastine, vincristine, leurosidine, vindesine, leurosine, paclitaxel and the like. Other useful antineoplastic agents include estramustine, carboplatin, cyclophosphamide, bleomycin, gemcitabine, ifosamide, melphalan, hexamethyl melamine, thiotepa, cytarabin, idatrexate, trimetrexate, dacarbazine, L-asparaginase, camptothecin, CPT-11, topotecan, ara-C, bicalutamide, 5 flutamide, leuprolide, pyridobenzoindole derivatives, interferons and interleukins.

Preferably, the pharmaceutical preparation is in unit dosage form. In such form, the preparation is subdivided into unit doses containing appropriate quantities of the active component, *e.g.*, an effective amount to achieve the desired purpose.

10 The quantity of active compound in a unit dose of preparation may be varied or adjusted from about 0.1 mg to 1000 mg, preferably from about 1 mg to 300 mg, more preferably 10 mg to 200 mg, according to the particular application.

The actual dosage employed may be varied depending upon the requirements of the patient and the severity of the condition being treated. Determination of the proper dosage for a particular situation is within the skill of the art. Generally, treatment is initiated with smaller 15 dosages which are less than the optimum dose of the compound. Thereafter, the dosage is increased by small amounts until the optimum effect under the circumstances is reached. For convenience, the total daily dosage may be divided and administered in portions during the day if desired.

The amount and frequency of administration of the HSP90 inhibitors used in the methods 20 of the present invention and, if applicable, other chemotherapeutic agents and/or radiation therapy will be regulated according to the judgment of the attending clinician (physician) considering such factors as age, condition and size of the patient as well as severity of the disease being treated. A dosage regimen of the HSP90 inhibitors can be intravenous administration of from 1 mg to 5gm/day, more preferably 10 mg to 2000 mg/day, more preferably still 10 to 1000 mg/day, and 25 most preferably 50 to 600 mg/day, in one or more (preferably two) doses, to block tumor growth.

The chemotherapeutic agent and/or radiation therapy can be administered according to therapeutic protocols well known in the art. It will be apparent to those skilled in the art that the administration of the chemotherapeutic agent and/or radiation therapy can be varied depending on the disease being treated and the known effects of the chemotherapeutic agent and/or radiation 30 therapy on that disease. Also, in accordance with the knowledge of the skilled clinician, the

therapeutic protocols (*e.g.*, dosage amounts and times of administration) can be varied in view of the observed effects of the administered therapeutic agents (*i.e.*, antineoplastic agent or radiation) on the patient, and in view of the observed responses of the disease to the administered therapeutic agents.

5 Also, in general, the HSP90 inhibitor and the chemotherapeutic agent do not have to be administered in the same pharmaceutical composition, and may, because of different physical and chemical characteristics, have to be administered by different routes. For example, the HSP90 inhibitor may be administered orally to generate and maintain good blood levels, while the chemotherapeutic agent may be administered intravenously. The determination of the mode of
10 administration and the advisability of administration, where possible, in the same pharmaceutical composition, is well within the knowledge of the skilled clinician. The initial administration can be made according to established protocols known in the art, and then, based upon the observed effects, the dosage, modes of administration and times of administration can be modified by the skilled clinician.

15 The particular choice of HSP90 inhibitor, and chemotherapeutic agent and/or radiation will depend upon the diagnosis of the attending physicians and their judgment of the condition of the patient and the appropriate treatment protocol.

 The HSP90 inhibitor, and chemotherapeutic agent and/or radiation may be administered concurrently (*e.g.*, simultaneously, essentially simultaneously or within the same treatment
20 protocol) or sequentially, depending upon the nature of the proliferative disease, the condition of the patient, and the actual choice of chemotherapeutic agent and/or radiation to be administered in conjunction (*i.e.*, within a single treatment protocol) with the HSP90 inhibitor.

 If the HSP90 inhibitor, and the chemotherapeutic agent and/or radiation are not administered simultaneously or essentially simultaneously, then the optimum order of
25 administration of the HSP90 inhibitor, and the chemotherapeutic agent and/or radiation, may be different for different tumors. Thus, in certain situations the HSP90 inhibitor may be administered first followed by the administration of the chemotherapeutic agent and/or radiation; and in other situations the chemotherapeutic agent and/or radiation may be administered first followed by the administration of the HSP90 inhibitor. This alternate administration may be
30 repeated during a single treatment protocol. The determination of the order of administration, and the number of repetitions of administration of each therapeutic agent during a treatment protocol,

is well within the knowledge of the skilled physician after evaluation of the disease being treated and the condition of the patient. For example, the chemotherapeutic agent and/or radiation may be administered first, especially if it is a cytotoxic agent, and then the treatment continued with the administration of the HSP90 inhibitor followed, where determined advantageous, by the administration of the chemotherapeutic agent and/or radiation, and so on until the treatment protocol is complete.

Thus, in accordance with experience and knowledge, the practicing physician can modify each protocol for the administration of a component (therapeutic agent-*i.e.*, HSP90 inhibitor, chemotherapeutic agent or radiation) of the treatment according to the individual patient's needs, as the treatment proceeds.

The attending clinician, in judging whether treatment is effective at the dosage administered, will consider the general well-being of the patient as well as more definite signs such as relief of disease-related symptoms, inhibition of tumor growth, actual shrinkage of the tumor, or inhibition of metastasis. Size of the tumor can be measured by standard methods such as radiological studies, *e.g.*, CAT or MRI scan, and successive measurements can be used to judge whether or not growth of the tumor has been retarded or even reversed. Relief of disease-related symptoms such as pain, and improvement in overall condition can also be used to help judge effectiveness of treatment.

EXAMPLES

The following examples are illustrative only, and are not intended to be limiting of the invention.

Example 1:

Cytotoxic Activity of 17AAG on K562 Versus a Normal Cell Type

Grosveld et al., Mol Cell Biol 6(2):607-16 (1986) showed that the chronic myelocytic cell line K562 produces a chimeric bcr/c-abl transcript, making it a suitable model system to demonstrate the methods of the invention. The cell line is widely available, *e.g.*, from American Type Culture Collection ("ATCC"; Manassas, VA, USA; cat# CCL-243) and can be propagated in a variety of media, *e.g.*, ATCC's Iscove's modified Dulbecco's medium with 4 mM L-glutamine adjusted to contain 1.5 g/L sodium bicarbonate, 90%; fetal bovine serum, 10%; 37C.

Experimental

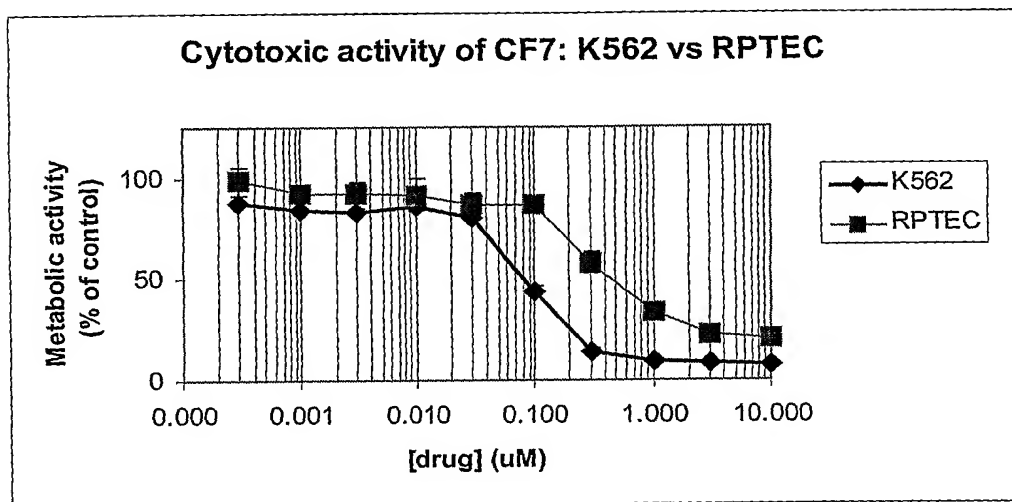
To K562 cells (suspension grown in DMEM media supplemented w/10% Fetal Bovine Serum (FBS) and 1mM HEPES; subcultured biweekly at 100K cells/ml) in a 96 well plate (0.1 ml medium; 2000 cells per well) were added various concentrations of 17-AAG (CF7) and the effects measured over a period of 3-6 days using an MTS assay protocol similar to that offered by Promega Corp (Madison, WI, US; cat# G5421).

The MTS assay is a colorimetric assay for determining the number of viable cells in proliferation, cytotoxicity or chemosensitivity assays. The CellTiter 96® AQueous Assay is composed of solutions of tetrazolium compound (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H- tetrazolium, inner salt; MTS) and an electron coupling reagent (phenazine methosulfate) PMS. MTS is bio-reduced by cells into a formazan that is soluble in tissue culture medium. Barltrop et al. (1991) Bioorg. & Med. Chem. Lett. 1, 611. The absorbance of the formazan at 490nm can be measured directly from 96 well assay plates without additional processing. Cory et al. (1991) Cancer Commun. 3, 207; Riss, T.L. and Moravec, R.A. (1992) Mol. Biol. Cell 3 (Suppl.), 184a. The conversion of MTS into the aqueous soluble formazan is accomplished by dehydrogenase enzymes found in metabolically active cells. The quantity of formazan product as measured by the amount of 490nm absorbance is directly proportional to the number of living cells in culture.

Using the MTS assay, cytotoxicity (defined as “growth inhibition” and not necessarily versus renal proximal tubular endothelial cells (normal cells) was determined as shown in the following Tables. “Sem” refers to standard error of the mean, which is calculated as the standard deviation divided by the square root of the sample size; the numbers reflect triplicate replicates. Dilutions of the compounds were prepared in DMSO and straight DMSO was used as a control corresponding to 100% metabolic activity.

Conc (uM)	Metabolic Activity			
	K562	sem1	RPTEC	sem1
10.0000	7.89	0.56	20.10	2.64
3.0000	8.12	1.02	22.01	2.49
1.0000	9.51	0.59	34.01	0.19
0.3000	14.40	1.53	58.03	5.09
0.1000	44.06	2.76	86.46	1.51
0.0300	80.12	2.29	86.40	5.96
0.0100	85.94	0.06	91.81	8.22
0.0030	83.00	2.25	92.73	4.79

0.0010	83.81	0.73	92.26	2.97
0.0003	88.00	0.40	98.69	7.16

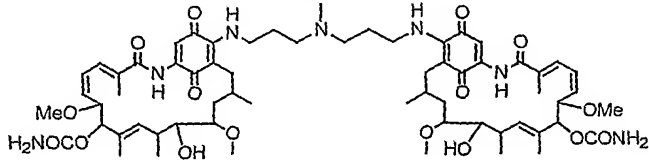
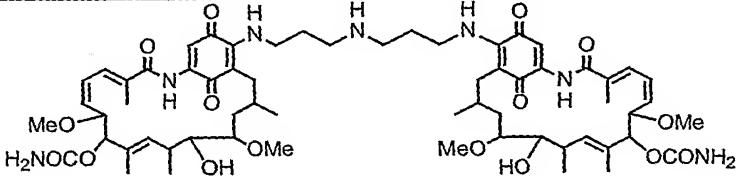
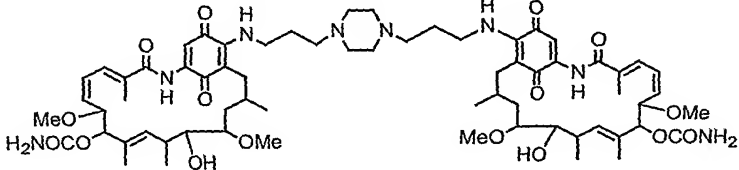
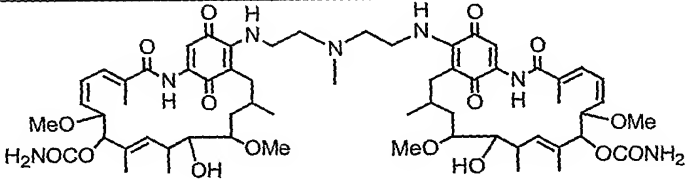
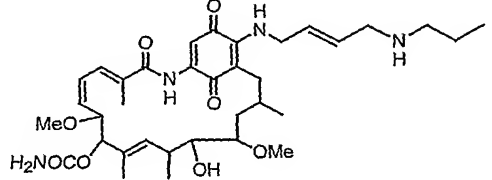


As demonstrated, the fusion protein cancer line K562 is more sensitive to the HSP90 inhibitor than is the normal cell line, RPTEC. It is expected that this will hold true for a variety of tumor cell lines versus a variety of normal cell lines.

In addition to the effects of 17-AAG on K562 versus RPTEC, the effects of a number of other putative HSP90 inhibitors and control compounds were tested side-by-side per the following Table, where "NEC" refers to no effective concentration.

Compound	RPTEC IC ₅₀ (nM)	K562 IC ₅₀ (nM)
CF7	400	70
DMSO	NEC	NEC
208	1000	50
237	4000	100
483	1000	70
481	4000	400

In the table, compound CF7 is the well known 17-AAG and compounds 207, 208, 237, 483, and 481 have the following formulas.

Compound #	Formula
208	 <p>a water soluble dimer</p>
237	 <p>a water soluble dimer</p>
207	 <p>a water soluble dimer</p>
483	 <p>a water soluble dimer</p>
481	 <p>a water soluble prodrug</p>

A separate study using the well known compound, radicicol, yielded results approximating those obtained for compound 237. Preparation of compounds 207, 208, 237, 483, and 481 is described in the following examples.

Example 2:

Preparation of Compound #208

3,3'-diamino-N-methyldipropylamine (1.32g, 9.1mmol) was added dropwise to a solution of Geldanamycin (10g, 17.83mmol) in DMSO (200ml) in a flame-dried flask under N₂ and stirred at room temperature. The reaction mixture was diluted with water after 12 hours. A precipitate was formed and filtered to give the crude product. The crude product was chromatographed by silica chromatography (5% CH₃OH/CH₂Cl₂) to afford the desired dimer as a purple solid (8.92g, 7.2mmol). Yield: 81%; mp 153°C (dec.); ¹H NMR (CDCl₃) δ 0.95 (d, J = 7 Hz, 6H, 2CH₃), 1.0 (d, J = 7 Hz, 6H, 2CH₃), 1.69 (m, 4 H, 2 CH₂), 1.74 (m, 4 H, 2CH₂), 1.76 (s, 6 H, 2 CH₃), 1.83 (m, 2H, 2CH), 2.0 (s, 6H, 2CH₃), 2.3 (s, 3H, N-CH₃), 2.36(dd, J = 14Hz, 2H, 2CH), 2.5 (m, 4H, 2CH₂), 2.63 (d, 2H, 2CH), 2.75(m, 2H, 2CH), 3.25(s, 6H, 2OCH₃), 3.35(s, 6H, 2OCH₃), 3.4 (m, 2H, 2CH), 3.50 (m, 4H, 2CH₂), 3.68(m, 2H, 2CH), 4.2(Bs, 2H, OH), 4.3(d, J = 10 Hz, 2H, 2CH), 4.8(Bs, 4H, 2NH₂), 5.19(s, 2H, 2CH), 5.82(t, J = 15 Hz, 2H, 2CH=), 5.89(d, J = 10 Hz, 2H, 2CH=), 6.59(t, J = 15 Hz, 2H, 2CH=), 6.92 (d, J = 10 Hz, 2H, 2CH=), 7.13 (t, 2H, 2NH), 7.24(s, 2H, 2CH=), 9.21(s, 2H, 2NH); MS (m/z)1203 (M+H).

The corresponding HCl salt was prepared by the following method: an HCl solution in EtOH (5 ml, 0.123N) was added to a solution of compound #208 (1 gm as prepared above) in THF (15 ml) and EtOH (50 ml) at room temperature. The reaction mixture was stirred for 10 min. The salt was precipitated, filtered and washed with large amount of EtOH and dried in vacuo.

Example 3:

Preparation of Compound #207

Compound #207 was prepared by the same method described in example 2 except that 1,4-bis (3-aminopropyl) piperazine was used instead of 3,3'-diamino-N-methyldipropylamine. The pure purple product was obtained after column chromatography (silica gel); yield: 90%; mp 162°C; ¹H NMR (CDCl₃) δ 0.97 (d, J = 6.6 Hz, 6H, 2CH₃), 1.0 (d, J = 6.6 Hz, 6H, 2CH₃), 1.73 (m, 4 H, 2 CH₂), 1.78 (m, 4 H, 2CH₂), 1.80 (s, 6 H, 2 CH₃), 1.85 (m, 2H, 2CH), 2.0 (s, 6H, 2CH₃), 2.4 (dd, J = 11Hz, 2H, 2CH), 2.55 (m, 8H, 4CH₂), 2.67 (d, J = 15 Hz, 2H, 2CH), 2.63 (t, J = 10 HZ, 2H, 2CH), 2.78(t, J = 6.5 Hz, 4H, 2CH₂), 3.26(s, 6H, 2OCH₃), 3.38(s, 6H, 2OCH₃), 3.4 (m, 2H, 2CH), 3.60 (m, 4H, 2CH₂), 3.75(m, 2H, 2CH), 4.6(d, J = 10 Hz, 2H, 2CH), 4.65 (Bs, 2H, 2OH), 4.8(Bs, 4H, 2NH₂), 5.19(s, 2H, CH), 5.83(t, J = 15 Hz, 2H, 2CH=), 5.89(d, J = 10 Hz, 2H, 2CH=), 6.58(t, J = 15 Hz, 2H, 2CH=), 6.94 (d, J = 10 Hz, 2H, 2CH=), 7.24(s, 2H, 2CH=), 7.60 (m, 2H, 2NH), 9.20(s, 2H, 2NH); MS (m/z) 1258 (M+H); The corresponding HCl salt was prepared by the same procedure as described in example 1.

Example 4:**Preparation of Compound #237**

Compound #237 was prepared by the same method described in example 2 except that 3,3'-diamino-dipropylamine was used instead of 3,3'-diamino-N-methyldipropylamine. The pure purple product was obtained after flash chromatography (silica gel); yield: 93%; mp 165°C; ¹H NMR (CDCl₃) δ 0.97 (d, J = 6.6 Hz, 6H, 2CH₃), 1.0 (d, J = 6.6 Hz, 6H, 2CH₃), 1.72 (m, 4 H, 2 CH₂), 1.78 (m, 4 H, 2CH₂), 1.80 (s, 6 H, 2 CH₃), 1.85 (m, 2H, 2CH), 2.0 (s, 6H, 2CH₃), 2.4 (dd, J = 11Hz, 2H, 2CH), 2.67 (d, J = 15 Hz, 2H, 2CH), 2.63 (t, J = 10 HZ, 2H, 2CH), 2.78(t, J = 6.5 Hz, 4H, 2CH₂), 3.26(s, 6H, 2OCH₃), 3.38(s, 6H, 2OCH₃), 3.4 (m, 2H, 2CH), 3.60 (m, 4H, 2CH₂), 3.75(m, 2H, 2CH), 4.6(d, J = 10 Hz, 2H, 2CH), 4.65 (Bs, 2H, 2OH), 4.8(Bs, 4H, 2NH₂), 5.19(s, 2H, 2CH), 5.83(t, J = 15 Hz, 2H, 2CH=), 5.89(d, J = 10 Hz, 2H, 2CH=), 6.58(t, J = 15 Hz, 2H, 2CH=), 6.94 (d, J = 10 Hz, 2H, 2CH=), 7.17 (m, 2H, 2NH), 7.24(s, 2H, 2CH=), 9.20(s, 2H, 2NH); MS (m/z)1189 (M+H); The corresponding HCl salt was prepared by the same procedure as described in example 1.

Example 5:**Preparation of Compound #483**

Compound #483 was prepared by the same method described in example 2 except that 2,2'-diamino-N-methyldiethylamine was used instead of 3,3'-diamino-N-methyldipropylamine. The pure purple product was obtained after flash chromatography; yield: 90%; mp 167-169 °C; ¹H NMR (CDCl₃) δ 0.95 (d, J = 7 Hz, 6H, 2CH₃), 1.00 (d, J = 7 Hz, 6H, 2CH₃), 1.85 (m, 4 H, 2CH₂), 1.75 (s, 6 H, 2 CH₃), 1.80 (m, 2H, 2CH), 2.0 (s, 6H, 2CH₃), 2.30 (s, 3H, N-CH₃), 2.30 (dd, J = 14Hz, 2H, 2CH), 2.5 (m, 4H, 2CH₂), 2.63 (d, 2H, 2CH), 2.75(m, 2H, 2CH), 3.25(s, 6H, 2OCH₃), 3.35(s, 6H, 2OCH₃), 3.4 (m, 2H, 2CH), 3.50 (m, 4H, 2CH₂), 3.68(m, 2H, 2CH), 4.2(Bs, 2H, OH), 4.30 (d, J = 10 Hz, 2H, 2CH), 4.8(Bs, 4H, 2NH₂), 5.19 (s, 2H, 2CH), 5.82 (t, J = 15 Hz, 2H, 2CH=), 5.90 (d, J = 10 Hz, 2H, 2CH=), 6.59(t, J = 15 Hz, 2H, 2CH=), 6.92 (d, J = 10 Hz, 2H, 2CH=), 7.13 (t, 2H, 2NH), 7.24 (s, 2H, 2CH=), 9.20 (s, 2H, 2NH); MS (m/z)1175 (M+H);); The corresponding HCl salt was prepared by the same procedure as described in example 1.

Example 6:**Preparation of Compound #481**

To 200 mg (0.357 mmol) of geldanamycin in 8 ml of dry THF in a flame-dried flask was added 91.6 mg (0.714 mmol) of N-propyl-1,4-diamino-2-butene drop-wise under nitrogen. The reaction mixture was stirred at room temperature for 4 h at which time TLC analysis indicated the reaction was complete. The solvent was removed by rotary evaporation and the crude material was chromatographed (5% CH₃OH/CH₂Cl₂ to 15% CH₃OH/CH₂Cl₂) to afford the desired compound as a purple solid (150 mg, 0.228 mmol); yield: 64%; mp 131°C; ¹H NMR (CDCl₃) δ 0.97 (m, 9H, 3CH₃), 1.52 (m, 2H, CH₂), 1.72 (m, 3H, CH + CH₂), 1.80 (s, 3H, CH₃), 2.0 (s, 3H, CH₃), 2.38 (dd, J = 11 Hz, 1H, CH), 2.72 (m, 4H, 2CH, CH₂), 3.26 (s, 3H, OCH₃), 3.38 (s, 3H, OCH₃), 3.46 (m, 1H, CH), 3.6 (m, 1H, CH), 4.18 (m, 4H, 2CH₂), 4.34 (d, J = 10 Hz, 1H, CH), 4.8 (bs, 2H, NH₂), 5.19 (s, 1H, CH), 5.88 (m, 4H, 4CH=), 6.38 (m, 1H, NH), 6.61 (t, J = 15 Hz, 1H, CH=), 6.94 (d, J = 10 Hz, 1H, CH=), 7.30 (s, 1H, CH=), 9.16 (s, 1H, NH); MS (m/z) 658 (M+H). The corresponding HCl salt was prepared by the same procedure as described in example 1.

* * *

Various patents, publications, and formulations are within the levels of ordinary skill in the art to which the invention pertains. All documents including the sequence listing cited in this disclosure are incorporated by reference to the same extent as if each reference had been incorporated by reference in its entirety individually, although none is admitted to be prior art.

One skilled in the art would readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The methods and compositions described herein as presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art, are encompassed within the spirit of the invention, and are defined by the scope of the claims.

It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention. Thus, such additional embodiments are within the scope of the present invention and the following claims.

The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms “comprising,” “consisting essentially of” and “consisting of” may be replaced with either of the other two terms. The terms and expressions
5 which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments, optional features,
10 modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the description and the appended claims.

In addition, where features or aspects of the invention are described in terms of Markush groups or other grouping of alternatives, those skilled in the art will recognize that the invention is
15 also thereby described in terms of any individual member or subgroup of members of the Markush group or other group, and exclusions of individual members as appropriate.

Claims

We claim:

1. A method of treating a patient having a genetically-defined disease characterized by a chromosomal aberration that yields an oncogenic fusion protein, comprising:
 - 5 providing a cell, tissue, or fluid sample of a patient suspected of having said genetically-defined disease;
 - identifying one or more characteristics indicative of said disease in or on said cell, tissue, or fluid sample; and
 - administering to said patient a pharmaceutically effective amount of an HSP90-
10 inhibiting compound.
2. The method of claim 1, wherein said compound is an ansamycin.
3. The method of claim 2, wherein said ansamycin is selected from the group consisting of geldanamycin, 17-AAG, herbimycin A, and macbecin.
4. The method of claim 2, wherein said ansamycin is 17-AAG.
- 15 5. The method of claim 1, wherein said compound is a compound that binds into the ATP-binding site of a HSP90.
- 6 The method of claim 5 wherein said compound is radicicol or an analog thereof.
7. The method of claim 1 wherein said identifying comprises using PCR or LCR to identify a nucleic acid encoding said oncogenic fusion protein.
- 20 8. The method of claim 1 wherein said identifying comprises using an antibody to identify said fusion protein.
9. The method of claim 1 wherein said identifying comprises using a cytochemical technique.
10. The method of claim 9 wherein said cytochemical technique employs nucleic acid
25 hybridization.

11. The method of claim 10 wherein said cytochemical technique is FISH.
12. The method of claim 1 wherein said disease is a hematopoietic disorder.
13. The method of claim 11 wherein said hematopoietic disorder is selected from the group consisting of a T or B cell lymphoma, CML, APL, ALL, AML, NHL, and CMML.
- 5 14. The method of claim 1 wherein said disease is characterized by a solid tumor.
15. The method of claim 14 wherein said solid tumor is selected from the group consisting of papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma, synovial sarcoma.
- 10 16. The method of claim 1 wherein said fusion protein contains one or more functional domains or portions thereof selected from the group consisting of kinases and DNA binding motifs.
17. The method of claim 12 or 13 wherein said administering employs an *ex vivo* procedure.
- 15 18. The method of claim 14 wherein said administering is intralesional.
19. The method of claim 1 wherein said administering is parenteral.
20. The method of claim 1 wherein said HSP90-inhibiting compound has an IC_{50} at least two-fold higher for cells that do not have characteristics indicative of said genetically-defined proliferative disorder relative to those cells that do have such
- 20 characteristics.
21. The method of claim 1 wherein said HSP90-inhibiting compound has an IC_{50} at least five-fold higher for cells that do not have characteristics indicative of said genetically-defined proliferative disorder relative to those cells that do have such characteristics.

22. The method of claim 1 wherein said HSP90-inhibiting compound has an IC_{50} at least ten-fold higher for cells that do not have characteristics indicative of said genetically-defined proliferative disorder relative to those cells that do have such characteristics.

23. The method of claim 1 wherein cells of said patient are monitored *in vitro* for sensitivity prior to administration of said compound to said patient.

24. The method of claim 1 wherein said non-random chromosomal aberration is a translocation.

25. The method of claim 1 wherein said non-random chromosomal aberration is a inversion.

26. The method of claim 1 wherein said non-random chromosomal aberration is a deletion.

27. The method of claim 1 wherein said non-random chromosomal aberration is selected from the group consisting of inv14 (q11; q32), t(9; 22)(q34; q11), t(1; 19)(q23; p13.3), t(17; 19)(q22; p13), t(15; 17)(q21-q11-22), t(11; 17)(q23; q21.1), t(4; 11)(q21; q23), t(9; 11)(q21; q23), t(11; 19)(q23; p13), t(X; 11)(q13; q23), t(1; 11)(p32; q23), t(6; 11)(q27; q23), t(11; 17)(q23; q21), t(8; 21)(q22; q22), t(3; 21)(q26; q22), 5(16; 21)(p11; q22), t(6; 9)(p23; q34), t(4; 16)(q26; p13), inv(2; 2)(p13; p11.2-14), inv(16)(p13q22), t(5; 12)(q33; p13), t(2; 5)(2p23; q35), t(9; 12)(q34;p13), del(12p), t(15; 17)(q22;q12), t(11; 17)(q23;q12), t(16; 16)(p13;q22), inv(16)(p13;q22), t(9; 11)(p22;q23), t(1; 22)(p13;q13), t(3; 3)(q21;q26), inv(3)(q21q26), t(3; 5)(q21;q31), t(3; 5)(q25;q34), t(7; 11)(p15;p15), t(8; 16)(p11;p13), t(9; 12)(q34;p13), t(12; 22)(p13;q13), del(5q), del(7q), del(20q), t(11q23), t(12; 21)(p13;q22), t(5; 12)(q31;p13), t(1; 12)(q25;p13), t(12; 15)(p13;q25), t(1; 12)(q21;p13), t(12; 21)(q13;p32), and t(5; 7)(q33;q11.2)).

28. The method of claim 1 wherein said non-random chromosomal aberration is a t(9; 22)(q34; q11) optionally characterized by and comprising a sequence selected from any one of SEQ ID NOs 15-26 or a homolog, isoform, or allelic variation thereof.

29. A method of treating cancerous cells in a heterogeneous population of cells, said heterogeneous population comprising both cancerous and noncancerous, and said

cancerous cells characterized by fusion proteins not found in said noncancerous cells, said method comprising:

administering to said heterogeneous population of cells a pharmaceutically effective amount of an HSP90-inhibiting compound.

5 30. The method of claim 29 wherein said compound has an IC_{50} that is at least five-fold lower for said cancerous cells than for said noncancerous cells within said heterogeneous population, and wherein said pharmaceutically effective amount administered is about one half or less of the IC_{50} of said noncancerous cells.

10 31. The method of claim 29 wherein said compound has an IC_{50} that is at least ten-fold lower for said cancerous cells than for said noncancerous cells within said heterogeneous population, and wherein said pharmaceutically effective amount administered is about one half or less of the IC_{50} of said noncancerous cells.

32. The method of any of claims 29-31, wherein said compound is an ansamycin.

15 33. The method of claim 32, wherein said ansamycin is selected from the group consisting of geldanamycin, 17-AAG, herbimycin A, and macbecin.

34. The method of claim 33, wherein said ansamycin is 17-AAG.

35. The method of any of claims 29-31 wherein said HSP90-inhibiting compound is a compound that binds the ATP-binding site of a HSP90.

20 36. The method of any of claims 29-31 wherein said cancerous cells are leukemic cells.

37. The method of claim 36 wherein said leukemic cells are selected from the group consisting of a T or B cell lymphoma, CML, APL, ALL, AML, NHL, and CMML.

25 38. The method of any of claims 29-31 wherein said treatment is monitored using one or more techniques selected from the group consisting of PCR, antibody staining, and nucleic acid hybridization, and wherein said techniques are selective for the presence of cancerous cells.

The method of any of claims 29-31 wherein said genetically-defined proliferative disorder is a solid tumor.

40. The method of claim 39 wherein said solid tumor is selected from the group consisting of papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma, and synovial sarcoma.
41. The method of any of claims 29-31 wherein said fusion protein contains one or more functional domains selected from the group consisting of kinases and DNA binding motifs.
42. The method of any of claims 29-31 wherein said administering employs an *ex vivo* procedure.
43. The method of any of claims 29-31 wherein said administering is intralesional.
44. The method of any of claims 29-31 wherein said administering is parenteral.
45. The method of claim 29 wherein said fusion protein arises from a chromosomal translocation.
46. The method of claim 29 wherein said fusion protein arises from a chromosomal inversion.
47. The method of claim 29 wherein said fusion protein arises from a chromosomal deletion.
48. The method of claim 29 wherein said fusion protein is generated from a non-random chromosomal aberration selected from the group consisting of inv14 (q11; q32), t(9; 22)(q34; q11), t(1; 19)(q23; p13.3), t(17; 19)(q22; p13), t(15; 17)(q21-q11-22), t(11; 17)(q23; q21.1), t(4; 11)(q21; q23), t(9; 11)(q21; q23), t(11; 19)(q23; p13), t(X; 11)(q13; q23), t(1; 11)(p32; q23), t(6; 11)(q27; q23), t(11; 17)(q23; q21), t(8; 21)(q22; q22), t(3; 21)(q26; q22), 5(16; 21)(p11; q22), t(6; 9)(p23; q34), t(4; 16)(q26; p13), inv(2; 2)(p13; p11.2-14), inv(16)(p13q22), t(5; 12)(q33; p13), t(2; 5)(2p23; q35), t(9; 12)(q34; p13), del(12p), t(15; 17)(q22; q12), t(11; 17)(q23; q12), t(16; 16)(p13; q22), inv(16)(p13; q22), t(9; 11)(p22; q23), t(1; 22)(p13; q13), t(3; 3)(q21; q26), inv(3)(q21q26), t(3; 5)(q21; q31), t(3; 5)(q25; q34), t(7; 11)(p15; p15), t(8; 16)(p11; p13), t(9; 12)(q34; p13), t(12; 22)(p13; q13),

39. The method of any of claims 29-31 wherein said genetically-defined proliferative disorder is a solid tumor.

40. The method of claim 39 wherein said solid tumor is selected from the group consisting of papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma, and synovial sarcoma.

41. The method of any of claims 29-31 wherein said fusion protein contains one or more functional domains selected from the group consisting of kinases and DNA binding motifs.

42. The method of any of claims 29-31 wherein said administering employs an *ex vivo* procedure.

43. The method of any of claims 29-31 wherein said administering is intralesional.

44. The method of any of claims 29-31 wherein said administering is parenteral.

45. The method of claim 29 wherein said fusion protein arises from a chromosomal translocation.

46. The method of claim 29 wherein said fusion protein arises from a chromosomal inversion.

47. The method of claim 29 wherein said fusion protein arises from a chromosomal deletion.

48. The method of claim 29 wherein said fusion protein is generated from a non-random chromosomal aberration selected from the group consisting of inv14 (q11; q32), t(9; 22)(q34; q11), t(1; 19)(q23; p13.3), t(17; 19)(q22; p13), t(15; 17)(q21-q11-22), t(11; 17)(q23; q21.1), t(4; 11)(q21; q23), t(9; 11)(q21; q23), t(11; 19)(q23; p13), t(X; 11)(q13; q23), t(1; 11)(p32; q23), t(6; 11)(q27; q23), t(11; 17)(q23; q21), t(8; 21)(q22; q22), t(3; 21)(q26; q22), 5(16; 21)(p11; q22), t(6; 9)(p23; q34), t(4; 16)(q26; p13), inv(2; 2)(p13; p11.2-14), inv(16)(p13q22), t(5; 12)(q33; p13), t(2; 5)(2p23; q35), t(9; 12)(q34; p13), del(12p), t(15; 17)(q22; q12), t(11; 17)(q23; q12), t(16; 16)(p13; q22), inv(16)(p13; q22), t(9; 11)(p22; q23), t(1; 22)(p13; q13), t(3; 3)(q21; q26), inv(3)(q21; q26), t(3; 5)(q21; q31), t(3; 5)(q25; q34), t(7; 11)(p15; p15), t(8; 16)(p11; p13), t(9; 12)(q34; p13), t(12; 22)(p13; q13),

del(5q), del(7q), del(20q), t(11q23), t(12;21)(p13;q22), t(5;12)(q31;p13), t(1;12)(q25;p13), t(12;15)(p13;q25), t(1;12)(q21;p13), t(12;21)(q13;p32), and t(5;7)(q33;q11.2)).

49. The method of claim 29 wherein said non-random chromosomal aberration is t(9;22)(q34;q11).

5 50. The method of claim 1 or 29 wherein said fusion protein has a heightened dependence on HSP90.

51. The method of claim 20 or 29 wherein said HSP90-inhibiting compound has an IC₅₀ that is lower for cancerous cells than for noncancerous cells.

52. The method of claim 5 or 35 wherein said inhibitor is a synthetic analog of geldanamycin.

10 53. A method of treating a patient having a proliferative disease associated with a mutant protein or cellular protein isoform dependent on HSP90, comprising:

providing a cell, tissue, or fluid sample of a patient suspected of having said proliferative disease;

15 identifying in said cell, tissue, or fluid sample one or more characteristics indicative of said mutant protein or cellular protein isoform; and

administering to said patient a pharmaceutically effective amount of an HSP90-inhibiting compound.

20 54. The method of claim 53 wherein said mutant protein or cellular protein isoform is selected from the group consisting of src, RET, p53, p51, p63, p73, and homologs and allelic variations thereof.

55. The method of claim 53 wherein said mutant protein or cellular protein isoform is a dominant negative mutant.

25 56. The method of claim 53 wherein said mutant protein or cellular protein isoform is a human p53 selected from the group consisting of N239S, C176R, and R213*, Y236delta, C176Y, M133T, G245D, E258K, 1-293delta, G245C, R248W, E258K, R282W, R175H,

R280K, V143A, R175H, P177S, H178P, H179R, R181P, 238-9delta, G245S, G245D, M246R, R248Q, R249S, R273H, R273C, R273L, and D281Y.

57. The method of claim 53 wherein said mutant protein or cellular protein isoform is a dominant positive mutant.

5 58. The method of claim 57 wherein said mutant protein or cellular protein isoform is a C176Y mutant.

59. The method of claim 53 wherein said patient is heterozygous for said mutant protein or cellular protein isoform.

60. The method of claim 59 wherein said mutant protein or cellular protein isoform is p53 and wherein said proliferative disease is rheumatoid arthritis.
10

61. The method of claim 53, wherein said compound is an ansamycin.

62. The method of claim 61, wherein said ansamycin is selected from the group consisting of geldanamycin, 17-AAG, herbimycin A, and macbecin.

63. The method of claim 62, wherein said ansamycin is 17-AAG.

15 64. The method of claim 53, wherein said inhibitor is a compound that binds into the ATP-binding site of a HSP90.

65. The method of claim 64 wherein said compound is radicicol or an analog thereof.

66. The method of claim 53 wherein said identifying comprises using at least one technique selected from the group consisting of nucleic acid hybridization, PCR, LCR, antibody staining, and immunoprecipitation to determine the presence of said mutant protein or cellular protein isoform.
20

67. The method of claim 53 wherein said administering employs an *ex vivo* procedure.

68. The method of claim 53 wherein said administering is intralesional.

69. The method of claim 53 wherein said administering is parenteral.

70. The method of claim 53 wherein said HSP90-inhibiting compound has an IC_{50} at least two-fold higher for cells that do not have characteristics indicative of said mutant protein or cellular protein isoform relative to those cells that do have such characteristics.

71. The method of claim 53 wherein said HSP90-inhibiting compound has an IC_{50} at least ten-fold higher for cells that do not have characteristics indicative of said mutant protein or cellular protein isoform relative to those cells that do have such characteristics.

72. The method of claim 53 wherein cells of said patient are monitored *in vitro* for sensitivity prior to administration of said compound to said patient.

73. A method of selectively treating cells that express a mutant protein or cellular protein isoform that gives rise to a proliferative disorder dependent on HSP90, said method comprising:

providing a population of cells in which at least some of said population express a mutant protein or cellular protein isoform that is differentially dependent on HSP90 for effect and gives rise to a proliferative disorder, and

administering to said population a pharmaceutically effective amount of an HSP90-inhibiting compound.

74. The method of claim 73 wherein said compound has an IC_{50} that is at least five-fold lower for said cells that express said mutant protein or cellular protein isoform than for those cells that do not, and wherein said pharmaceutically effective amount administered is about one half or less of the IC_{50} of cells that do not express said mutant protein or cellular protein isoform.

75. The method of claim 73 wherein said compound has an IC_{50} that is at least ten-fold lower for said cells that express said mutant protein or cellular protein isoform than for those cells that do not, and wherein said pharmaceutically effective amount administered is about one half or less of the IC_{50} of cells that do not express said mutant protein or cellular protein isoform..

76. The method according to any of claims 73-75, wherein said compound is an ansamycin.

77. The method of claim 76, wherein said ansamycin is selected from the group consisting of geldanamycin, 17-AAG, herbimycin A, or macbecin.
78. The method of claim 77, wherein said ansamycin is 17-AAG.
79. The method of any of claims 73-75, wherein said compound is a compound that
5 binds the ATP-binding site of a HSP90.
80. The method of claim 79 wherein said compound is radicicol or an analog thereof.
81. The method of any of claims 73-75 wherein said treatment is monitored using one or more techniques selected from the group consisting of PCR, LCR, nucleic acid hybridization, antibody labeling, and immunoprecipitation, and wherein said techniques
10 are selective for the presence of said mutant protein or cellular protein isoform.
82. The method of any of claims 73-75 wherein said administering employs an *ex vivo* procedure.
83. The method of any of claims 73-75 wherein said administering is intralesional.
84. The method of any of claims 73-75 wherein said administering is parenteral.
- 15 85. The method of claim 76 wherein said HSP90-inhibiting compound has an IC_{50} that is lower for cells expressing the mutant protein or cellular protein isoform than for cells that do not express said mutant protein or cellular protein isoform.
86. The method of claim 64 or 73 wherein said inhibitor is a synthetic analogue of geldanamycin.
- 20 87. The method of claim 73 wherein said mutant protein or cellular protein isoform is selected from the group consisting of src, RET, p53, p51, p63, p73, and homologs and allelic variations thereof.
88. The method of claim 73 wherein said mutant protein or cellular protein isoform is a dominant negative mutant.

89. The method of claim 88 wherein said mutant protein or cellular protein isoform is a human p53 selected from the group consisting of N239S, C176R, and R213*, Y236delta, C174Y, M133T, G245D, E258K, 1-293delta, G245C, R248W, E258K, R282W, R175H, R280K, V143A, R175H, P177S, H178P, H179R, R181P, 238-9delta, G245S, G245D,
5 M246R, R248Q, R249S, R273H, R273C, R273L, and D281Y.
90. The method of claim 73 wherein said mutant protein or cellular protein isoform is a dominant positive mutant.
91. The method of claim 90 wherein said mutant protein or cellular protein isoform is C176Y human p53, or a homolog thereof.
- 10 92. The method of claim 73 wherein said cells that express a mutant protein or cellular protein isoform are heterozygous for said mutant protein or cellular protein isoform.
93. The method of claim 92 wherein said mutant protein or cellular protein isoform is p53 and wherein said proliferative disease is rheumatoid arthritis or a cancer.

FIGURE 1

<u>Type of Aberration</u>	<u>Background Literature</u>	<u>Affected Gene(s)</u>	<u>Protein Domain</u>	<u>Fusion Protein</u>	<u>Disease</u>
t(9; 22)(q34; q11)	de Klein, A. et al. Nature 300, 765-767 (1982)	<i>CABL</i> (9q34) <i>BCR</i> (22q11)	tyrosine kinase serine kinase	serine + tyrosine kinase	CML/ALL
inv14 (q11; q32)	Baer, R., Chen, K.-C., Smith, S. D. & Rabbitts, T. H. Cell 43, 705-713 (1985); Denny, C. T. et al. Nature 320, 549-551 (1986)	TCR- α (14q11) VH-(14q32)	TCR-C α Ig VH	VH-TCR-C α	T/B-cell lymphoma
t(1; 19)(q23; p13.3)	Kamps, M. P., Murre, C., Sun, X.-H. & Baltimore, D. Cell 60, 547-555 (1990); Nourse, J. et al. Cell 60, 535-545 (1990)	<i>PBX1</i> (1q23) <i>E2A</i> (19p13.3)	HD AD-b-HLH	AD + HD	pre-B-ALL
t(17; 19)(q22; p13)	Hunger, S. P., Ohyashiki, K., Toyama, K. & Clearly, M. L. Genes Dev. 6, 1608-1620 (1992); Inaba, T. et al. Science 257, 531-534 (1992)	<i>HLF</i> (17q22) <i>E2A</i> (19p13)	bZIP AD-b-HLH	AD + bZIP	pro-B-ALL
t(15; 17)(q21-q11-22)	Giliard, E. F. & Solomon, E. Sem. Cancer Biol. 4, 359-368 (1993)	<i>PML</i> (15Q21) <i>RARA</i> (17q21)	Zinc-finger Retinoic acid receptor- α	Zinc-finger + RAR DNA and ligand binding	APL
t(11; 17)(q23; q21.1)	Chen, Z. et al. EMBO J. 12, 1161-1167 (1993)	<i>PLZF</i> (11q23) <i>RARA</i> (17q21)	Zinc-finger Retinoic acid receptor- α	Zn-finger + RAR DNA and ligand binding	APL
t(4; 11)(q21; q23)	Djabali, M. et al. Nature Genet. 2, 113-118 (1992); Gu, Y. et al. Cell 71, 701-708 (1992)	<i>MLL</i> (11q23) <i>AF4</i> (4q21)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + (Ser-pro)	ALL/preB- ALL/ ANLL
t(9; 11)(q21; q23)	Nakamura, T. et al. Proc. natn. Acad. Sci. U.S.A. 90, 4631-4635 (1993); Lida, S. et al. Oncogene 8, 3085-3092 (1993)	<i>MLL</i> (11q23) <i>AF9/MLLT3</i> (9p22)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + (Ser-Pro)	ALL/preB- ALL/ ANLL
t(11; 19)(q23; p13)	Tkachuk, D. C., Kohler, S. & Cleary, M. L. Cell 71, 691-700 (1992); Yamamoto, K. et al. Oncogene 8, 2617-2625 (1993)	<i>MLL</i> (11q23) <i>ENL</i> (19p13)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + Ser-Pro	pre-B-ALL/ T-ALL/ ANLL

FIGURE 1 (Cont'd)

<u>Type of Aberration</u>	<u>Background Literature</u>	<u>Affected Gene(s)</u>	<u>Protein Domain</u>	<u>Fusion Protein</u>	<u>Disease</u>
t(X; 11)(q13; q23)	Corral, J. et al. Proc. natn. Acad. Sci. U.S.A. 90, 8538-8542 (1993)	<i>MLL</i> (11q23) <i>AFX1</i> (Zq13)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + (Ser-Pro)	T-ALL
t(1; 11)(p32; q23)	Bernard, O. A., Mauchauffe, M., Mecucci, C., Van Den Berghe, H. & Berger, R. Oncogene 9, 1039-1045 (1994)	<i>MLL</i> (11q23) <i>AF1P</i> (1p32)	A-T hook/Zn-finger Eps-15 homologue	A-T hook +	ALL
t(6; 11)(q27; q23)	Prasac, R. et al. Cancer Res. 53, 5624-5628 (1993)	<i>MLL</i> (11q23) <i>AF6</i> (6q27)	A-T hook/Zn-finger myosin homologue	A-T hook +	ALL
t(11; 17)(q23; q21)	Prasac, R. et al. Proc. natn. Acad. Sci. U.S.A. 91, 8107-8111 (1994)	<i>MLL</i> (11q23) <i>AF17</i> (17q21)	A-T hook/Zn-finger Cys-rich/leucine zipper	A-T hook + leucine zipper	AML
t(8; 21)(q22; q22)	Ohki, M. Sem. Cancer Biol. 4, 369-376 (1993)	<i>AML1/CBFα</i> (21q22) <i>ETO/MTG8</i> (8q22)	DNA binding/runt homology Zn-finger	DNA binding + Zn-fingers	AML
t(3; 21)(q26; q22)	Mitani, K. et al. EMBO J. 13, 504-510 (1994)	<i>AML1</i> (21q22) <i>EVI-1</i> (3q26)	DNA binding Zn-finger	DNA binding + Zn-fingers	CML
t(3; 21)(q26; q22)	Nucifora, G., Begy, C. R., Erickson, P., Drackin, H. A. & Rowley, J. D. Proc. natn. Acad. Sci. U.S.A. 90, 7784-7788 (1993)	<i>AML1</i> (21q22) <i>EAP</i> (3q26)	DNA binding Sn protein	DNA binding + out-of-frame EAP	Myelo-dysplasia
5(16; 21)(p11; q22)	Shimizu, K. et al. Proc. natn. Acad. Sci. U.S.A. 90, 10280-10284 (1993)	<i>FUS</i> (16p11) <i>ERG</i> (21q22)	Gin-Ser Tyr/Gly-rich/RNA binding Ets-like DNA binding	Gin-Ser-Tyr + DNA binding	Myeloid
t(6; 9)(p23; q34)	von Lindern, M. et al. Molec. Cell Biol. 12, 1687-1697 (1992)	<i>DEK</i> (6p23) <i>CAN</i> (9q34)	unknown ZIP	ZIP+	AML
9; 9?	von Lindern, M., Breems, D., van Baai, S., Acriansen, H. & Grosveld, G. Genes Chrom. Cancer 5, 227-234 (1992)	<i>SET</i> (9q34) <i>CAN</i> (9p34)	ZIP	ZIP+	AUL
t(4; 16)(q26; p13)	Laabi, Y. et al. EMBO J. 11, 3897-3904 (1992)	<i>IL-2</i> (4q26) <i>BCM</i> (16p13.1)	IL2 TM domain	IL-2/TM	T-lymphoma

FIGURE 1 (Cont'd)

<u>Type of Aberration</u>	<u>Background Literature</u>	<u>Affected Gene(s)</u>	<u>Protein Domain</u>	<u>Fusion Protein</u>	<u>Disease</u>
inv(2; 2)(p13; p11.2-14)	Lu, D. et al. Oncogene 6, 1235-1241 (1991)	REL (2p13) NRG (2p11.2-14)	DNA binding-activator not known	DNA binding +	NHL
inv(16)(p13q22)	Liu, P. et al. Science 261, 1041-1044 (1993)	Myosin MYH11 (16p13) CBF- β (16q22)		DNA binding?	AML
t(5; 12)(q33; p13)	Golub, T. R., Barker, G. F., Lovett, M. & Gilliland, D. G. Cell 77, 307-316 (1994)	PDGF- β (5q33) TEL (12p13)	Receptor kinase Ets-like DNA binding	Kinase + DNA binding	CMML
t(2; 5)(2p23; q35)	Morris, S. W. et al. Science 263, 1281-1284 (1994)	NPM (5q35) ALK (2p23)	Nuclear phosphoprotein Tyrosine kinase	N terminus NPM + kinase	NHL
t(11; 22)(q24; q12)	Delattre, O. et al. Nature 359, 162-165 (1992)	FLII (11q24) EWS (22q12)	Ets-like DNA binding Gin-Ser-Tyr/Gly- rich/RNA binding	Gin-Ser-Tyr + DNA binding	Ewing's sarcoma
inv10(q11.2; q21)	Pierotti, M. A. et al. Proc. natn. Acad. Sci. U.S.A. 89, 1616-1620 (1992)	RET (10q11.2) D10S170 (q21)	tyrosine kinase uncharacterized	Unk + tyrosine kinase	Papillary thyroid carcinoma
t(12; 22)(q13; q12)	Zucman, J. et al. Nature Genet. 4, 341-345 (1993)	ATF1 (12q13) EWS (22q12)	bZIP Gln-Ser-Tyr/Gly- rich/RNA binding	Gin-Ser-Tyr + bZIP	a melanoma
t(12; 16)(q13; p11)	Crozat, A., Aman, P., Mandahl, N. & Ron, D. Nature 363, 640-644 (1993); Rabbitts, T. H. ; Forster, A., Larson, R. & Nathan, P. Nature Genet. 4, 175-180 (1993)	CHOP (12q13) FUS (16p11)	(DNA binding?)/ZIP Gln-Ser-Tyr/Gly- rich/RNA binding	Gin-Ser-Tyr +(DNA binding?)/ZIP	Liposarcoma
t(2; 13)(q35; q14)	Ben-David, Y., Giddens, E. B., Letwin, K. & Bernstein, A. Genes Dev. 5, 908-918 (1991)	PAX3 (2q35) FKHR (13q14)	Paired box/homeodomain Forkhead domain	PB/HD +DNA binding	Rhabdomyosarcoma
t(X; 18)(p11.2;q11.2)	Clark, J. et al. Nature Genet. 7, 502-5087 (1994)	SYT (18q11.2) SSX (Xp11.2)	None identified None identified		Synovial sarcoma

SEQUENCE LISTING

<110> CONFORMA THERAPEUTICS CORP.

<120> METHODS FOR TREATING GENETICALLY-DEFINED PROLIFERATIVE
DISORDERS WITH HSP90 INHIBITORS

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<210> 4

<211> 284

<212> PRT

<213> Homo sapiens

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          20          25          30

Phe Gln Met Val Asp Glu Leu Glu Ala Val Pro Asn Ile Pro Leu Val
          35          40          45

Pro Asp Glu Glu Leu Asn Ala Leu Lys Ile Lys Ile Ser Gln Ile Lys
          50          55          60

Ser Asp Ile Gln Arg Glu Lys Arg Ala Asn Lys Gly Ser Lys Ala Thr
          65          70          75          80

Glu Arg Leu Lys Lys Lys Leu Ser Glu Gln Glu Ser Leu Leu Leu Leu
          85          90          95

Met Ser Pro Ser Met Ala Phe Arg Val His Ser Arg Asn Gly Lys Ser
          100          105          110

Tyr Thr Phe Leu Ile Ser Ser Asp Tyr Glu Arg Ala Glu Trp Arg Glu
          115          120          125

Asn Ile Arg Glu Gln Gln Lys Lys Cys Phe Arg Ser Phe Ser Leu Ala
          130          135          140

Ser Val Glu Leu Gln Met Leu Thr Asn Ser Cys Val Lys Leu Gln Thr
          145          150          155          160

Val His Ser Ile Pro Leu Thr Ile Asn Lys Glu Asp Asp Glu Ser Pro
          165          170          175

Gly Leu Tyr Gly Phe Leu Asn Val Ile Val His Ser Ala Thr Gly Phe
          180          185          190

Lys Gln Ser Ser Lys Leu Gln Arg Pro Val Ala Ser Asp Phe Glu Pro
          195          200          205

Gln Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser Lys Glu Asn Leu Leu
          210          215          220

Ala Gly Pro Ser Glu Asn Asp Pro Asn Leu Phe Val Ala Leu Tyr Asp
          225          230          235          240

Phe Val Ala Ser Gly Asp Asn Thr Leu Ser Ile Thr Lys Gly Glu Lys

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255

Thr Lys Asn Gly Gln Gly Trp Val Pro Ser Asn Tyr
275 280

Gly Ser Lys Ala Thr Glu Arg Leu Lys Lys Lys Leu Ser Glu Gln Glu

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20	25	30
Ser Leu Leu Leu Leu Met Ser Pro Ser Met Ala Phe Arg Val His Ser		
35	40	45
Arg Asn Gly Lys Ser Tyr Thr Phe Leu Ile Ser Ser Asp Tyr Glu Arg		
50	55	60
Ala Glu Trp Arg Glu Asn Ile Arg Glu Gln Gln Lys Lys Cys Phe Arg		
65	70	75
Ser Phe Ser Leu Ala Ser Val Glu Leu Gln Met Leu Thr Asn Ser Cys		
85	90	95
Val Lys Leu Gln Thr Val His Ser Ile Pro Leu Thr Ile Asn Lys Glu		
100	105	110
Asp Asp Glu Ser Pro Gly Leu Tyr Gly Phe Leu Asn Val Ile Val His		
115	120	125
Ser Ala Thr Gly Phe Lys Gln Ser Ser Lys Leu Gln Arg Pro Val Ala		
130	135	140
Ser Asp Phe Glu Pro Gln Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser		
145	150	155
Lys Glu Asn Leu Leu Ala Ala Pro Ser Glu Asn Asp Pro Asn Leu Phe		
165	170	175
Val Ala Leu Tyr Asp Phe Val Ala Ser Gly Asp Asn Thr Leu Ser Ile		
180	185	190
Thr Lys Gly Glu Lys Leu Arg Val Leu Gly Tyr Asn His Asn Gly Glu		
195	200	205
Trp Cys Glu Ala Gln Thr Lys Ile Gly Gln Gly Trp Val Pro Ser Asn		
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Tyr		
225		

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<211> 679

<212> DNA

<213> Homo sapiens

<400> 8

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<211> 332

<212> PRT

<213> Homo sapiens

<400> 9

Ala Asn Lys Gly Ser Lys Ala Thr Glu Arg Leu Lys Lys Lys Leu Ser
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 20 25 30

Val His Ser Arg Asn Gly Lys Ser Tyr Thr Phe Leu Ile Ser Ser Asp
 35 40 45

Tyr Glu Arg Ala Glu Trp Arg Glu Asn Ile Arg Glu Gln Gln Lys Lys
 50 55 60

Cys Phe Arg Ser Phe Ser Leu Thr Ser Val Glu Leu Gln Met Leu Thr
 65 70 75 80

Asn Ser Cys Val Lys Leu Gln Thr Val His Ser Ile Pro Leu Thr Ile
 85 90 95

Asn Lys Glu Asp Asp Glu Ser Pro Gly Leu Tyr Gly Phe Leu Asn Val
 100 105 110

Ile Val His Ser Ala Thr Gly Phe Lys Gln Ser Ser Lys Ala Leu Gln
 115 120 125

Arg Pro Val Ala Ser Asp Phe Glu Pro Gln Gly Leu Ser Glu Ala Ala
 130 135 140

Arg Trp Asn Ser Lys Glu Asn Leu Leu Ala Gly Pro Ser Glu Asn Asp
 145 150 155 160

Pro Asn Leu Phe Val Ala Leu Tyr Asp Phe Val Ala Ser Gly Asp Asn
 165 170 175

Thr Leu Ser Ile Thr Lys Gly Glu Lys Leu Arg Val Leu Gly Tyr Asn
 180 185 190

His Asn Gly Glu Trp Cys Glu Ala Gln Thr Lys Asn Gly Gln Gly Trp
 195 200 205

Val Pro Ser Asn Tyr Ile Thr Pro Val Asn Ser Leu Glu Lys His Ser
 210 215 220

Trp Tyr His Gly Pro Val Ser Arg Asn Ala Ala Glu Tyr Leu Leu Ser
 225 230 235 240

Ser Gly Ile Asn Gly Ser Phe Leu Val Arg Glu Ser Glu Ser Ser Pro
 245 250 255

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Gly Gln Arg Ser Ile Ser Leu Arg Tyr Glu Gly Arg Val Tyr His Tyr
 260 265 270

Arg Ile Asn Thr Ala Ser Asp Gly Lys Leu Tyr Val Ser Ser Glu Ser
 275 280 285

Arg Phe Asn Thr Leu Ala Glu Leu Val His His His Ser Thr Val Ala
 290 295 300

Asp Gly Leu Ile Thr Thr Leu His Tyr Pro Ala Pro Lys Arg Asn Lys
 305 310 315 320

Pro Thr Val Tyr Gly Val Ser Pro Asn Tyr Asp Lys
 325 330

<210> 10

<211> 997

<212> DNA

<213> Homo sapiens

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 tacacgttcc tgatctcctc tgactatgag cgtgcagagt ggagggagaa catccgggag 180
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<210> 11

<211> 101

<212> PRT

<213> Homo sapiens

<400> 11

Arg Glu Gln Gln Lys Lys Cys Phe Arg Ser Phe Ser Leu Thr Ser Val
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Glu Leu Gln Met Leu Thr Asn Ser Cys Val Lys Leu Gln Thr Val His
 20 25 30

Ser Ile Pro Leu Thr Ile Asn Lys Glu His Asp Glu Ser Pro Gly Leu
 35 40 45

Tyr Gly Phe Leu Asn Val Ile Val His Ser Ala Thr Gly Phe Lys Gln
 50 55 60

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Ser Ser Asn Leu Tyr Cys Thr Leu Glu Val Asp Ser Phe Gly Tyr Phe
 65 70 75 80

Val Asn Lys Ala Lys Thr Arg Val Tyr Arg Asp Thr Ala Glu Pro Asn
 85 90 95

Leu Leu Ala Gly Pro
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<210> 12
 <211> 305
 <212> DNA
 <213> Homo sapiens

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 ggaacatgat gagtctccgg ggctctatgg gtttctgaat gtcacgtcc actcagccac 180
 tggatttaag cagagttcaa atctgtactg caccctggag gtggattcct ttgggtattt 240
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 accca 305

<210> 13
 <211> 250
 <212> DNA
 <213> Homo sapiens

<400> 13
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<210> 14
 <211> 63
 <212> DNA
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<210> 15
 <211> 21
 <212> PRT
 <213> Homo sapiens

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Pro Pro Gly Tyr Gly

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20

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<211> 63
<212> DNA
<213> Homo sapiens

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ggc 63

<210> 17
<211> 21
<212> PRT
<213> Homo sapiens

<400> 17
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1 5 10 15
Val Ala Ser Asp Phe
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<210> 18
<211> 63
<212> DNA
<213> Homo sapiens

<400> 18
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ttt 63

<210> 19
<211> 140
<212> PRT
<213> Homo sapiens

<400> 19
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1 5 10 15
His Asp Leu Leu Lys His Thr Pro Ala Ser His Pro Asp His Pro Leu
20 25 30
Leu Gln Asp Ala Leu Arg Ile Ser Gln Asn Phe Leu Ser Ser Ile Asn
35 40 45
Glu Glu Ile Thr Pro Arg Arg Gln Ser Met Thr Val Lys Lys Gly Glu
50 55 60
Gly Glu Asp Arg Met Lys Ala Ser Ser Thr Arg Lys Arg Leu Leu Leu
65 70 75 80
Met Glu Glu Ala Leu Gln Arg Pro Val Ala Ser Asp Phe Glu Pro Gln

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	85		90		95
Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser Lys Glu Asn Leu Leu Ala					
	100		105		110
Gly Pro Ser Glu Asn Asp Pro Asn Leu Phe Val Ala Leu Tyr Asp Phe					
	115		120		125
Val Ala Ser Gly Asp Asn Thr Leu Ser Ile Thr Lys					
	130		135		140

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 <211> 423
 <212> DNA
 <213> Homo sapiens

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 aag 423

<210> 21
 <211> 307
 <212> PRT
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<400> 21
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 20 25 30
 Val His Ser Arg Asn Gly Lys Ser Tyr Thr Phe Leu Ile Ser Ser Asp
 35 40 45
 Tyr Glu Arg Ala Glu Trp Arg Glu Asn Ile Arg Glu Gln Gln Lys Lys
 50 55 60
 Cys Phe Arg Ser Phe Ser Leu Thr Ser Val Glu Leu Gln Met Leu Thr
 65 70 75 80
 Asn Ser Cys Val Lys Leu Gln Thr Val His Ser Ile Pro Leu Thr Ile
 85 90 95
 Asn Lys Glu Glu Ala Leu Gln Arg Pro Val Ala Ser Asp Phe Glu Pro
 100 105 110
 Gln Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser Lys Glu Asn Leu Leu
 115 120 125

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Ala Gly Pro Ser Glu Asn Asp Pro Asn Leu Phe Val Ala Leu Tyr Asp
 130 135 140

Phe Val Ala Ser Gly Asp Asn Thr Leu Ser Ile Thr Lys Gly Glu Lys
 145 150 155 160

Leu Arg Val Leu Gly Tyr Asn His Asn Gly Glu Trp Cys Glu Ala Gln
 165 170 175

Thr Lys Asn Gly Gln Gly Trp Val Pro Ser Asn Tyr Ile Thr Pro Val
 180 185 190

Asn Ser Leu Glu Lys His Ser Trp Tyr His Gly Pro Val Ser Arg Asn
 195 200 205

Ala Ala Glu Tyr Leu Leu Ser Ser Gly Ile Asn Gly Ser Phe Leu Val
 210 215 220

Arg Glu Ser Glu Ser Ser Pro Gly Gln Arg Ser Ile Ser Leu Arg Tyr
 225 230 235 240

Glu Gly Arg Val Tyr His Tyr Arg Ile Asn Thr Ala Ser Asp Gly Lys
 245 250 255

Leu Tyr Val Ser Ser Glu Ser Arg Phe Asn Thr Leu Ala Glu Leu Val
 260 265 270

His His His Ser Thr Val Ala Asp Gly Leu Ile Thr Thr Leu His Tyr
 275 280 285

Pro Ala Pro Lys Arg Asn Lys Pro Thr Val Tyr Gly Val Ser Pro Asn
 290 295 300

Tyr Asp Lys
 305

<210> 22

<211> 922

<212> DNA

<213> Homo sapiens

<400> 22

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 cagcagaaga agtgtttcag aagctttctcc ctgacatccg tggagctgca gatgctgacc 240
 aactcgtgtg tgaaactcca gactgtccac agcattccgc tgaccatcaa taaggaagaa 300
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922

<210> 23

<211> 359

<212> PRT

<213> Homo sapiens

<400> 23

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 20 25 30

Arg Leu Thr Trp Pro Arg Arg Ser Tyr Ser Pro Arg Ser Phe Glu Asp
 35 40 45

Cys Gly Gly Gly Tyr Thr Pro Asp Cys Ser Ser Asn Glu Asn Leu Thr
 50 55 60

Ser Ser Glu Glu Asp Phe Ser Ser Gly Gln Ser Ser Arg Val Ser Pro
 65 70 75 80

Ser Pro Thr Thr Tyr Arg Met Phe Arg Asp Lys Ser Arg Ser Pro Ser
 85 90 95

Gln Asn Ser Gln Gln Ser Phe Asp Ser Ser Ser Pro Pro Thr Pro Gln
 100 105 110

Cys His Lys Arg His Arg His Cys Pro Val Val Val Ser Glu Ala Thr
 115 120 125

Ile Val Gly Val Arg Lys Thr Gly Gln Ile Trp Pro Asn Asp Gly Glu
 130 135 140

Gly Ala Phe His Gly Asp Ala Glu Ala Leu Gln Arg Pro Val Ala Ser
 145 150 155 160

Asp Phe Glu Pro Gln Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser Lys
 165 170 175

Glu Asn Leu Leu Ala Gly Pro Ser Glu Asn Asp Pro Asn Leu Phe Val
 180 185 190

Ala Leu Tyr Asp Phe Val Ala Ser Gly Asp Asn Thr Leu Ser Ile Thr
 195 200 205

Lys Gly Glu Lys Leu Arg Val Leu Gly Tyr Asn His Asn Gly Glu Trp
 210 215 220

Cys Glu Ala Gln Thr Lys Asn Gly Gln Gly Trp Val Pro Ser Asn Tyr
 225 230 235 240

Ile Thr Pro Val Asn Ser Leu Glu Lys His Ser Trp Tyr His Gly Pro
 245 250 255

Val Ser Arg Asn Ala Ala Glu Tyr Leu Leu Ser Ser Gly Ile Asn Gly

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260 265 270
 Ser Phe Leu Val Arg Glu Ser Glu Ser Ser Pro Gly Gln Arg Ser Ile
 275 280 285
 Ser Leu Arg Tyr Glu Gly Arg Val Tyr His Tyr Arg Ile Asn Thr Ala
 290 295 300
 Ser Asp Gly Lys Leu Tyr Val Ser Ser Glu Ser Arg Phe Asn Thr Leu
 305 310 315 320
 Ala Glu Leu Val His His His Ser Thr Val Ala Asp Gly Leu Ile Thr
 325 330 335
 Thr Leu His Tyr Pro Ala Pro Lys Arg Asn Lys Pro Thr Val Tyr Gly
 340 345 350
 Val Ser Pro Asn Tyr Asp Lys
 355

<210> 24
 <211> 1079
 <212> DNA
 <213> Homo sapiens

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<210> 25
 <211> 34
 <212> PRT
 <213> Homo sapiens

<400> 25
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 20 25 30

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Asn Gly

<210> 26
 <211> 106
 <212> DNA
 <213> Homo sapiens

<400> 26
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 gagacgcagg taaaagcccc ggtcttaggc taaatcacia tgggga 106

<210> 27
 <211> 114
 <212> PRT
 <213> Homo sapiens

<400> 27
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 Arg Leu Trp Ala Trp Glu Lys Phe Val Tyr Leu Asp Glu Lys Gln His
 20 25 30
 Ala Trp Leu Pro Leu Thr Ile Glu Ile Lys Asp Arg Leu Gln Leu Arg
 35 40 45
 Val Leu Leu Arg Arg Glu Asp Val Val Leu Gly Arg Pro Met Thr Pro
 50 55 60
 Thr Gln Ile Gly Pro Ser Leu Leu Pro Ile Met Trp Gln Leu Tyr Pro
 65 70 75 80
 Asp Gly Arg Tyr Arg Ser Ser Asp Ser Ser Phe Trp Arg Leu Val Tyr
 85 90 95
 His Ile Lys Ile Asp Gly Val Glu Asp Met Leu Leu Glu Leu Leu Pro
 100 105 110

Asp Asp

<210> 28
 <211> 1324
 <212> DNA
 <213> Homo sapiens

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cctgcccgtg aacacgcctg caaacgcgtg ctgcccacac aggttcacgt gcagctcaag 960
gaaaggcctg aaaggagccc ttatctgtgc tcaggactca gaagcctctg ggtcagtgg 1020
ccacatcccg ggacgcagca ggaggccagg ccggcgagcc ctgtggatga gccctcagaa 1080
cccttggtt gccacgtgg aaaagggata gaggttgggt ttccccctt tatagatgg 1140
cacgcacctg ggtgttaca agttgtatgt ggcataaata ctttttgtaa tgattgatta 1200
aatgcaagat agtttatcta acttcgtgcg caatcagctt ctatccttga cttagattct 1260
ggtggagaga agtgagaata ggcagcccc aaataaaaaa tattcatgga aaaaaaaaaa 1320
aaaa 1324

```

<210> 29

<211> 114

<212> PRT

<213> Homo sapiens

<400> 29

```

Met Ala Glu Cys Pro Thr Leu Gly Glu Ala Val Thr Asp His Pro Asp
  1             5             10             15

```

```

Arg Leu Trp Ala Trp Glu Lys Phe Val Tyr Leu Asp Glu Lys Gln His
      20             25             30

```

```

Ala Trp Leu Pro Leu Thr Ile Glu Ile Lys Asp Arg Leu Gln Leu Arg
      35             40             45

```

```

Val Leu Leu Arg Arg Glu Asp Val Val Leu Gly Arg Pro Met Thr Pro
      50             55             60

```

```

Thr Gln Ile Gly Pro Ser Leu Leu Pro Ile Met Trp Gln Leu Tyr Pro
      65             70             75             80

```

```

Asp Gly Arg Tyr Arg Ser Ser Asp Ser Ser Phe Trp Arg Leu Val Tyr
      85             90             95

```

```

His Ile Lys Ile Asp Gly Val Glu Asp Met Leu Leu Glu Leu Leu Pro
      100            105            110

```

Asp Asp

<210> 30

<211> 1324

<212> DNA

<213> Homo sapiens

<400> 30

```

cttgagaggc tctggctctt gcttcttagg cggccccgagg acgccatggc cgagtgtccc 60
acactcgggg aggcatcac cgaccacccg gaccgcctgt gggcctggga gaagttcgtg 120
tatttggaag agaagcagca cgctggctg cccttaacca tcgagataaa ggatagggtta 180
cagttacggg tgctcttgcg tcgggaagac gtcgtcctgg ggaggcctat gacccccacc 240

```

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```

cagataggcc caagcctgct gcctatcatg tggcagctct accctgatgg acgataccga 300
tcctcagact ccagtttctg gcgcttagtg taccacatca agattgacgg cgtggaggac 360
atgcttctcg agctgctgcc agatgactga tgtatggtct tggcagcacc tgtctccttt 420
cacccagggg cctgagcctg gccagcctac aatggggatg ttgtgtttct gttcaccttc 480
gtttactatg cctgtgtctt ctccaccacg ctgggggtctg ggaggaatgg acagacagag 540
gatgagctct acccagggcc tgcaggacct gcctgtagcc cactctgctc gccttagcac 600
taccactcct gccaaaggagg attccatttg gcagagcttc ttccagggtgc ccagctatac 660
ctgtgcctcg gcttttctca gctggatgat ggtcttcagc ctctttctgt cccttctgtc 720
cctcacagca ctagtatttc atgttgacac cccactcagc tccgtgaact tgtgagaaca 780
cagccgattc acctgagcag gacctctgaa accctggacc agtgggtctca catgggtgcta 840
cgctgcatg taaacacgcc tgcaaacgct gcctgccggt aaacacgcct gcaaacgctg 900
cctgcccgtg aacacgcctg caaacgctgc ctgcccacac aggttcacgt gcagctcaag 960
gaaaggcctg aaaggagccc ttatctgtgc tcaggactca gaagcctctg ggtcagtggt 1020
ccacatcccg ggacgcagca ggaggccagg ccggcgagcc ctgtggatga gccctcagaa 1080
cccttggtt gccacgtgg aaaagggata gaggttgggt ttccccctt tatagatggt 1140
cacgcacctg ggtgttataa agttgtatgt ggcataaata ctttttgtaa tgattgatta 1200
aatgcaagat agtttatcta acttcgtgcg caatcagctt ctatccttga cttagattct 1260
ggtggagaga agtgagaata ggcagccccc aaataaaaaa tattcatgga aaaaaaaaaa 1320
aaaa                                             1324

```

<210> 31
 <211> 560
 <212> DNA
 <213> Homo sapiens

```

<400> 31
gtcgactgtg agttcccagc agaggcccag agtcccggtc cggcagccga ggggaagcggg 60
ggggtcttcc agaagaagaa agggccaagg tcaccccggg gcctctccag cagcagcaga 120
gggcggcggt cgggtgtcgt gctggccggg gcctcgagga aggcgcgggc cagctggggc 180
cgggtctgctg ttcccaggag ctgccaccgt tccagggagc aagtcaggcc gggacgttag 240
cgctgcgcg ggacctcac ttgccaccaa ggaccccaca aaccccgccc catccttagc 300
gcctgcgcgg gacctcact tgccaccaag acccccacaa accccgcccc atcctgcctt 360
acgccccgcc ccaaggctgt tctcccgacc cggggtcccc cccaagacc gtcctccgcg 420
ccgcgcgtt ggtggcggcc gcatgctgcc cggatataaa gggtcggccc cacatcccag 480
ggaccagcga gcggccttga gaggtctctg ctcttgcttc ttaggcggcc cgaggacgcc 540
atggccgagt gcccgacact                                     560

```

<210> 32
 <211> 125
 <212> PRT
 <213> Homo sapiens

```

<400> 32
Phe Ala Gly Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly
  1              5              10             15

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
      20              25              30

Phe Thr Phe Ser Ser Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly
      35              40              45

Lys Gly Leu Val Trp Val Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr
      50              55              60

Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn

```


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65		70		75		80
Ala Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp						
	85		90			95
Thr Ala Val Tyr Tyr Cys Ala Arg Asp Pro Thr Gly Gly Ser Tyr Ile						
	100		105			110
Pro Thr Phe Gly Arg Gly Thr Ser Leu Ile Val His Pro						
	115		120			125

<210> 33
 <211> 375
 <212> DNA
 <213> Homo sapiens

<400> 33
 tttgcaggtg tccagtgtga ggtgcagctg gtggagtccg ggggaggctt agttcagcct 60
 ggggggtccc tgagactctc ctgtgcagcc tctggattca ccttcagtag ctactggatg 120
 cactgggtcc gccaaagctcc agggaagggg ctggtgtggg tctcacgtat taatagtgat 180
 gggagtagca caagctacgc ggactccgtg aagggccgat tcaccatctc cagagacaac 240
 gccagaaca cgctgtatct gcaaataaac agtctgagag ccgaggacac ggctgtgtat 300
 tactgtgcaa gagatccaac aggaggaagc tacataccta catttggaag aggaaccagc 360
 cttattgttc atccg 375

<210> 34
 <211> 125
 <212> PRT
 <213> Homo sapiens

<400> 34
 Thr Gly Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
 1 5 10 15
 Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr
 20 25 30
 Ser Ile Ser Ser Gly Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly
 35 40 45
 Lys Gly Leu Glu Trp Ile Gly Ser Ile Tyr His Ser Gly Ser Thr Tyr
 50 55 60
 Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser
 65 70 75 80
 Lys Asn Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr
 85 90 95
 Ala Val Tyr Tyr Cys Ala Arg Val Arg Arg Arg Tyr Ser Ser Ala Ser
 100 105 110
 Lys Ile Ile Phe Gly Ser Gly Thr Arg Leu Ser Ile Arg
 115 120 125

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<210> 35
 <211> 377
 <212> DNA
 <213> Homo sapiens

<400> 35
 tcacaggggt cctgtcccag gtgcagctgc aggagtcggg cccaggactg gtgaagcctt 60
 cggagaccct gtccctcacc tgcactgtct ctgggttactc catcagcagt gggttactact 120
 ggggctggat ccggcagccc ccagggaagg ggctggagtg gattgggagt atctatcata 180
 gtgggagcac ctactacaac ccgtccctca agagtcgagt caccatatca gtagacacgt 240
 ccaagaacca gttctccctg aagctgagct ctgtgaccgc cgcagacacg gccgtgtatt 300
 actgtgcgag agtccgtcgg aggtacagca gtgcttccaa gataatcttt ggatcaggga 360
 ccagactcag catccgg 377

<210> 36
 <211> 140
 <212> PRT
 <213> Homo sapiens

<400> 36
 Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
 1 5 10 15
 Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys
 20 25 30
 Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile
 35 40 45
 Ser Ser Gly Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly
 50 55 60
 Leu Glu Trp Ile Gly Ser Ile Tyr His Ser Gly Ser Thr Tyr Tyr Asn
 65 70 75 80
 Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn
 85 90 95
 Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
 100 105 110
 Tyr Tyr Cys Ala Arg Val Arg Arg Arg Tyr Ser Ser Ala Ser Lys Ile
 115 120 125
 Ile Phe Gly Ser Gly Thr Arg Leu Ser Ile Arg Pro
 130 135 140

<210> 37
 <211> 675
 <212> DNA
 <213> Homo sapiens

<400> 37
 ccacccacat gcaaactctc acttaggcgc ccacaggaag ccacaacaca tttccttaaa 60
 ttcaggtcca actcataagg gaaatgcttt ctgagagtca tggacctcct gtgcaagaac 120
 atgaagcacc tgtgggtttt cctcctgctg gtggcagctc ccagatgtga gtgtctcagg 180

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```

gatccagacg tgaagatatg ggaagtgcct ctgatcccag ggctcaccgt ggggtttttct 240
gttcacaggg gtcctgtccc aggtgcagct gcaggagtcg ggcccaggac tggatgaagcc 300
ttcggagacc ctgtccctca cctgcactgt ctctgggttac tccatcagca gtggttacta 360
ctggggctgg atccggcagc cccaggggaa ggggctggag tggattggga gtatctatca 420
tagtgggagc acctactaca acccgtcctt caagagtcga gtcaccatat cagtagacac 480
gtccaagaac cagttctccc tgaagctgag ctctgtgacc gccgcagaca cggccgtgta 540
ttactgtgcg agagtccgtc ggaggtacag cagtgtcttc aagataatct ttggatcagg 600
gaccagactc agcatccggc caagtaagta gaatgaagca ggagagcaag ggaggacgga 660
caactatttc ttctt 675

```

<210> 38

<211> 158

<212> PRT

<213> Homo sapiens

<400> 38

```

Met Val Thr Gly Gly Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly
  1              5              10              15

```

```

Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val
          20              25              30

```

```

Ser Gly Tyr Ser Ile Ser Ser Gly Tyr Tyr Trp Gly Trp Ile Arg Gln
    35              40              45

```

```

Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Ser Ile Tyr His Ser Gly
    50              55              60

```

```

Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val
    65              70              75              80

```

```

Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala
          85              90              95

```

```

Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Val Arg Arg Arg Tyr Ser
    100              105              110

```

```

Ser Ala Ser Lys Ile Ile Phe Gly Ser Gly Thr Arg Leu Ser Ile Arg
    115              120              125

```

```

Pro Asn Ile Gln Asn Pro Asp Pro Ala Val Tyr Gln Leu Arg Asp Ser
    130              135              140

```

```

Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr Asp Phe Asp
    145              150              155

```

<210> 39

<211> 508

<212> DNA

<213> Homo sapiens

<400> 39

```

tgtcctctga aaactcggga atttgtcact gaaatgggtga caggaggggt cctgtcccag 60
gtgcagctgc aggagtcggg cccaggactg gtgaagcctt cggagaccct gtccctcacc 120
tgcactgtct ctggttactc catcagcagt gggttactact ggggctggat ccggcagccc 180
ccaggggaagg ggctggagtg gattgggagt atctatcata gtgggagcac ctactacaac 240

```

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```

ccgtccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg 300
aagctgagct ctgtgaccgc cgcagacacg gccgtgtatt actgtgcgag agtccgctcg 360
aggtacagca gtgcttccaa gataatcttt ggatcaggga ccagactcag catccggcca 420
aatatccaga accctgaccc tgccgtgtac cagctgagag actctaaatc cagtgacaag 480
tctgtctgcc tattcaccga ttttgatt                               508

```

<210> 40

<211> 162

<212> PRT

<213> Homo sapiens

<400> 40

```

Met Ala Glu Ala Leu His Gly Lys Arg Val Leu Ser Gln Val Gln Leu
  1              5              10              15

Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu
          20          25          30

Ala Cys Thr Val Ser Gly Tyr Ser Ile Ser Ser Gly Tyr Tyr Trp Gly
      35          40          45

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Ser Ile
      50          55          60

Tyr His Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser Arg Val
      65          70          75          80

Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys Leu Ser
          85          90          95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Val Arg
      100          105          110

Arg Arg Tyr Ser Ser Ala Ser Lys Ile Ile Phe Gly Ser Gly Thr Arg
      115          120          125

Leu Ser Ile Arg Pro Asn Ile Gln Asn Pro Asp Pro Ala Val Tyr Gln
      130          135          140

Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr Asp
      145          150          155          160

Phe Asp

```

<210> 41

<211> 616

<212> DNA

<213> Homo sapiens

<400> 41

```

tgtcctctga aaactcggga atttgtcact gaaatgggtga caggagccta cagggtggcag 60
atgagaactc tcaacacagt tgtgttagaa gaaggatttc ctagagagac cctgactcaa 120
tgatgataca tggctgaagc attgcatgga aaacgggtcc tgtcccagggt gcagctgcag 180
gagtcggggcc caggactggt gaagccttcg gagaccctgt ccctcgccctg cactgtctct 240
ggttactcca tcagcagtggt ttactactgg ggctggatcc ggcagccccc aggggaagggg 300
ctgggagtga ttgggagtat ctatcatagt gggagcacct actacaaccc gtccctcaag 360

```

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```

agtcgagtca ccatatcagt agacacgtcc aagaaccagt tctccctgaa gctgagctct 420
gtgaccgccg cagacacggc cgtgtattac tgtgcgagag tccgtcggag gtacagcagt 480
gcttccaaga taatcttttg atcagggacc agactcagca tccggccaaa tatccagaac 540
cctgaccctg ccgtgtacca gctgagagac tctaaatcca gtgacaagtc tgtctgcta 600
ttcaccgatt ttgatt                                     616

```

<210> 42

<211> 550

<212> PRT

<213> Homo sapiens

<400> 42

```

Gly Tyr Gln Leu His Gly Ala Glu Val Asn Gly Gly Leu Pro Ser Ala
  1              5              10              15

Ser Ser Phe Ser Ser Ala Pro Gly Ala Thr Tyr Gly Val Ser Ser His
      20              25              30

Thr Pro Pro Val Ser Gly Ala Asp Ser Leu Leu Gly Ser Arg Gly Thr
      35              40              45

Thr Ala Gly Ser Ser Gly Asp Ala Leu Gly Lys Ala Leu Ala Ser Ile
      50              55              60

Tyr Ser Pro Asp His Ser Ser Asn Asn Phe Ser Ser Ser Pro Ser Thr
      65              70              75              80

Pro Val Gly Ser Pro Gln Gly Leu Ala Gly Thr Ser Gln Trp Pro Arg
      85              90              95

Ala Gly Ala Pro Gly Ala Leu Ser Pro Ser Tyr Asp Gly Gly Leu His
      100             105             110

Gly Leu Gln Ser Lys Ile Glu Asp His Leu Asp Glu Ala Ile His Val
      115             120             125

Leu Arg Ser His Ala Val Gly Thr Ala Gly Asp Met His Thr Leu Leu
      130             135             140

Pro Gly His Gly Ala Leu Ala Ser Gly Phe Thr Gly Pro Met Ser Leu
      145             150             155             160

Gly Gly Arg His Ala Gly Leu Val Gly Gly Ser His Pro Glu Asp Gly
      165             170             175

Leu Ala Gly Ser Thr Ser Leu Met His Asn His Ala Ala Leu Pro Ser
      180             185             190

Gln Pro Gly Thr Leu Pro Asp Leu Ser Arg Pro Pro Asp Ser Tyr Ser
      195             200             205

Val Leu Ser Ile Arg Gly Ala Gln Glu Glu Glu Pro Thr Asp Pro Gln
      210             215             220

Leu Met Arg Leu Asp Asn Met Leu Leu Ala Glu Gly Val Ala Gly Pro
      225             230             235             240

```

Glu	Lys	Gly	Gly	Gly	Ser	Ala	Ala	Ala	Ala	Ala	Ala	Ala	Ala	Ala	Ser
			245						250			255			
Gly	Gly	Ala	Gly	Ser	Asp	Asn	Ser	Val	Glu	His	Ser	Asp	Tyr	Arg	Ala
			260						265			270			
Lys	Leu	Ser	Gln	Ile	Arg	Gln	Ile	Tyr	His	Thr	Glu	Leu	Glu	Lys	Tyr
			275						280			285			
Glu	Gln	Ala	Cys	Asn	Glu	Phe	Thr	Thr	His	Val	Met	Asn	Leu	Leu	Arg
			290						295			300			
Glu	Gln	Ser	Arg	Thr	Arg	Pro	Ile	Ser	Pro	Lys	Glu	Ile	Glu	Arg	Met
			305						310			315			
Val	Ser	Ile	Ile	His	Arg	Lys	Phe	Ser	Ser	Ile	Gln	Met	Gln	Leu	Lys
			325						330			335			
Gln	Ser	Thr	Cys	Glu	Ala	Val	Met	Ile	Leu	Arg	Ser	Arg	Phe	Leu	Asp
			340						345			350			
Ala	Arg	Arg	Lys	Arg	Arg	Asn	Phe	Asn	Lys	Gln	Ala	Thr	Glu	Ile	Leu
			355						360			365			
Asn	Glu	Tyr	Phe	Tyr	Ser	His	Leu	Ser	Asn	Pro	Tyr	Pro	Ser	Glu	Glu
			370						375			380			
Ala	Lys	Glu	Glu	Leu	Ala	Lys	Lys	Cys	Gly	Ile	Thr	Val	Ser	Gln	Val
			385						390			395			
Ser	Asn	Trp	Phe	Gly	Asn	Lys	Arg	Ile	Arg	Tyr	Lys	Lys	Asn	Ile	Gly
			405						410			415			
Lys	Phe	Gln	Glu	Glu	Ala	Asn	Ile	Tyr	Ala	Ala	Lys	Thr	Ala	Val	Thr
			420						425			430			
Ala	Thr	Asn	Val	Ser	Ala	His	Gly	Ser	Gln	Ala	Asn	Ser	Pro	Ser	Thr
			435						440			445			
Pro	Asn	Ser	Ala	Gly	Ser	Ser	Ser	Ser	Phe	Asn	Met	Ser	Asn	Ser	Gly
			450						455			460			
Asp	Leu	Phe	Met	Ser	Val	Gln	Ser	Leu	Asn	Gly	Asp	Ser	Tyr	Gln	Gly
			465						470			475			
Ala	Gln	Val	Gly	Ala	Asn	Val	Gln	Ser	Gln	Val	Asp	Thr	Leu	Arg	His
			485						490			495			
Val	Ile	Ser	Gln	Thr	Gly	Gly	Tyr	Ser	Asp	Gly	Leu	Ala	Ala	Ser	Gln
			500						505			510			
Met	Tyr	Ser	Pro	Gln	Gly	Ile	Ser	Ala	Asn	Gly	Gly	Trp	Gln	Asp	Ala
			515						520			525			
Thr	Thr	Pro	Ser	Ser	Val	Thr	Ser	Pro	Thr	Glu	Gly	Pro	Gly	Ser	Val
			530						535			540			
His	Ser	Asp	Thr	Ser	Asn										

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545

550

<210> 43

<211> 2049

<212> DNA

<213> Homo sapiens

<400> 43

```

ggctaccagc tgcattggagc agaggtgaac ggagggctcc catctgcac ctccttctcc 60
tcagcccccg gagccacgta cggcgtctcc agccacacgc cgcctgtcag cggggccgac 120
agcctcctgg gctcccagag gaccacagct ggcagctccg gggatgccct cggcaaaagca 180
ctggcctcga tctactcccc ggatcactca agcaataact tctcgtccag cccttctacc 240
cccggtgggt cccccaggg cctggcagga acgtcacagt ggcctcgagc aggagcccc 300
gggtgccttat cggccagcta cgacgggggt ctccacggcc tgcagagtaa gatagaagac 360
cacctggacg aggccatcca cgtgctccgc agccacgccc tgggcacagc cggcgacatg 420
cacacgctgc tgcctggcca cggggcgtg gcctcaggtt tcaccggccc catgtcactg 480
ggcggggcgg acgcaggcct ggttggaggc agccacccc aggacggcct cgcaggcagc 540
accagcctca tgcacaacca cgcggccctc cccagccagc caggcacctc ccctgacctg 600
tctcggcctc ccgactccta cagtgttttg agtatccgag gagccagga ggaggaaccc 660
acagaccccc agctgatgag gctggacaac atgctgttag cgggaaggcg ggcggggcct 720
gagaagggcg gagggtcggc ggcagcggcg gcagcggcgg cggcttcttg aggggcaggt 780
tcagacaact cagtggagca ttcagattac agagccaaac tctcacagat cagacaaatc 840
taccatacgg agctggagaa atacgagcag gcctgcaacg agttcaccac ccacgtgatg 900
aatctcctgc gagagcaaag ccggaccagg cccatctccc caaaggagat tgagcggatg 960
gtcagcatca tccaccgcaa gtccagctcc atccagatgc agctcaagca gagcacgtgc 1020
gagggcggta tgatcctgag ttcccgatth ctggatgcgc ggcggaagag acggaatttc 1080
aacaagcaag cgacagaaat cctgaatgaa tatttctatt cccatctcag caacccttac 1140
cccagtgagg aagccaaaga ggagttagcc aagaagtgtg gcacacagt ctcccaggta 1200
tcaaactggt ttggaaataa gcgaatccgg tacaagaaga acataggtta atttcaagag 1260
gaagccaata tttatgctgc caaaacagct gtcactgcta ccaatgtgtc agcccatgga 1320
agccaagcta actcgccctc aactcccaac tcggctgggt cttccagttc ttttaacatg 1380
tcaaactctg gagatttggt catgagcgtg cagtcaactca atggggattc ttaccaaggg 1440
gcccagggtg gagccaacgt gcaatcacag gtggataccc ttccgcatgt tatcagccag 1500
acaggaggat acagtgatgg actcgcagcc agtcagatgt acagtccgca gggcatcagt 1560
gctaattggag gttggcagga tgctactacc ccttcacatg tgacctcccc tacagaaggc 1620
cctggcagtg ttcactctga tacctccaac tgatctccca gcaatcgcat ccgggctgac 1680
cctgtgcccc agttgggggca ggggcaggag ggagggtttc tctcccaacg ctgaagcggg 1740
cagactggag gtcgaagcaa tcagcaaaca caataagagt ctcttctct tctcttcttt 1800
gggatgctat ttcagccaat ctggacactt ctttatactc tcttcccttt tttttctggg 1860
tagaagccac ccttccctgc ctccagctgt cagcctgggt ttcgtcatct tccctgcccc 1920
tgtgcctctg tcctagactc ccggggtccc cgcctctct catatcactg aaggatattt 1980
tcaacaattg aaggaattta aagagcaaaa aaattacaaa gaaaataata aaagtgtttg 2040
tacgttttc 2049

```

<210> 44

<211> 574

<212> PRT

<213> Homo sapiens

<400> 44

```

Met Asn Gln Pro Gln Arg Met Ala Pro Val Gly Thr Asp Lys Glu Leu
  1                      5                      10                      15

Ser Asp Leu Leu Asp Phe Ser Met Met Phe Pro Leu Pro Val Thr Asn
                20                      25                      30

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Gly	Lys	Gly 35	Arg	Pro	Ala	Ser	Leu 40	Ala	Gly	Ala	Gln	Phe 45	Gly	Gly	Ser
Gly	Leu 50	Glu	Asp	Arg	Pro	Ser 55	Ser	Gly	Ser	Trp	Gly 60	Ser	Gly	Asp	Gln
Ser 65	Ser	Ser	Ser	Phe	Asp 70	Pro	Ser	Arg	Thr	Phe 75	Ser	Glu	Gly	Thr	His 80
Phe	Thr	Glu	Ser	His 85	Ser	Ser	Leu	Ser	Ser 90	Ser	Thr	Phe	Leu	Gly 95	Pro
Gly	Leu	Gly	Gly 100	Lys	Ser	Gly	Glu	Arg 105	Gly	Ala	Tyr	Ala	Ser	Phe	Gly
Arg	Asp	Ala 115	Gly	Val	Gly	Gly	Leu 120	Thr	Gln	Ala	Gly	Phe 125	Leu	Ser	Gly
Glu 130	Leu	Ala	Leu	Asn	Ser	Pro 135	Gly	Pro	Leu	Ser	Pro 140	Ser	Gly	Met	Lys
Gly 145	Thr	Ser	Gln	Tyr	Tyr 150	Pro	Ser	Tyr	Ser	Gly 155	Ser	Ser	Arg	Arg	Arg 160
Ala	Ala	Asp	Gly	Ser 165	Leu	Asp	Thr	Gln	Pro 170	Lys	Lys	Val	Arg	Lys 175	Val
Pro	Pro	Gly	Leu 180	Pro	Ser	Ser	Val	Tyr 185	Pro	Pro	Ser	Ser	Gly 190	Glu	Asp
Tyr	Gly	Arg 195	Asp	Ala	Thr	Ala	Tyr 200	Pro	Ser	Ala	Lys	Thr 205	Pro	Ser	Ser
Thr 210	Tyr	Pro	Ala	Pro	Phe	Tyr 215	Val	Ala	Asp	Gly	Ser 220	Leu	His	Pro	Ser
Ala 225	Glu	Leu	Trp	Ser	Pro 230	Pro	Gly	Gln	Ala	Gly 235	Phe	Gly	Pro	Met	Leu 240
Gly	Gly	Gly	Ser	Ser 245	Pro	Leu	Pro	Leu	Pro 250	Pro	Gly	Ser	Gly	Pro 255	Val
Gly	Ser	Ser	Gly 260	Ser	Ser	Ser	Thr	Phe 265	Gly	Gly	Leu	His	Gln	His	Glu
Arg	Met	Gly 275	Tyr	Gln	Leu	His 280	Gly	Ala	Glu	Val	Asn 285	Gly	Gly	Leu	Pro
Ser	Ala 290	Ser	Ser	Phe	Ser	Ser 295	Ala	Pro	Gly	Ala	Thr 300	Tyr	Gly	Gly	Val
Ser 305	Ser	His	Thr	Pro	Pro 310	Val	Ser	Gly	Ala	Asp 315	Ser	Leu	Leu	Gly	Ser
Arg	Gly	Thr	Thr	Ala 325	Gly	Ser	Ser	Gly	Asp 330	Ala	Leu	Gly	Lys	Ala 335	Leu
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340	345	350
Pro Ser Thr Pro Val Gly Ser Pro Gln Gly Leu Ala Gly Thr Ser Gln		
355	360	365
Trp Pro Arg Ala Gly Ala Pro Gly Ala Leu Ser Pro Ser Tyr Asp Gly		
370	375	380
Gly Leu His Gly Leu Gln Ser Lys Ile Glu Asp His Leu Asp Glu Ala		
385	390	395
Ile His Val Leu Arg Ser His Ala Val Gly Thr Ala Gly Asp Met His		
405	410	415
Thr Leu Leu Pro Gly His Gly Ala Leu Ala Ser Gly Phe Thr Ser Pro		
420	425	430
Met Ser Leu Gly Gly Arg His Ala Gly Leu Val Gly Gly Ser His Pro		
435	440	445
Glu Asp Gly Leu Ala Gly Ser Thr Ser Leu Met His Asn His Ala Ala		
450	455	460
Leu Pro Ser Gln Pro Gly Thr Leu Pro Asp Leu Ser Arg Pro Pro Asp		
465	470	475
Ser Tyr Ser Gly Gln Gly Ile Ser Pro Gln Leu Gly Pro Leu Ser Thr		
485	490	495
Ser Ile Tyr Leu Leu Thr Gln Asp Asp Lys Tyr Trp Ala Arg Arg Arg		
500	505	510
Lys Asn Asn Met Ala Ala Lys Arg Ser Arg Asp Ala Arg Arg Leu Lys		
515	520	525
Glu Asn Gln Ile Ala Ile Arg Ala Ser Phe Leu Glu Lys Glu Asn Ser		
530	535	540
Ala Leu Arg Gln Glu Val Ala Asp Leu Arg Lys Glu Leu Gly Lys Cys		
545	550	555
Lys Asn Ile Leu Ala Lys Tyr Glu Ala Arg His Gly Pro Leu		
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<210> 45

<211> 4410

<212> DNA

<213> Homo sapiens

<400> 45

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<210> 46

<211> 416

<212> PRT

<213> Homo sapiens

<400> 46

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                20                      25                      30

Pro Pro Leu Pro Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys
                35                      40                      45

Ser Ser Gly Tyr His Tyr Gly Val Ser Ala Cys Glu Gly Cys Lys Gly
  50                      55                      60

Phe Phe Arg Arg Ser Ile Gln Lys Asn Met Val Tyr Thr Cys His Arg
  65                      70                      75                      80

Asp Lys Asn Cys Ile Ile Asn Lys Val Thr Arg Asn Arg Cys Gln Tyr
                85                      90                      95

Cys Arg Leu Gln Lys Cys Phe Glu Val Gly Met Ser Lys Glu Ser Val
                100                      105                      110

Arg Asn Asp Arg Asn Lys Lys Lys Lys Glu Val Pro Lys Pro Glu Cys
  115                      120                      125

Ser Glu Ser Tyr Thr Leu Thr Pro Glu Val Gly Glu Leu Ile Glu Lys
  130                      135                      140

Val Arg Lys Ala His Gln Glu Thr Phe Pro Ala Leu Cys Gln Leu Gly
  145                      150                      155                      160

Lys Tyr Thr Thr Asn Asn Ser Ser Glu Gln Arg Val Ser Leu Asp Ile
                165                      170                      175

Asp Leu Trp Asp Lys Phe Ser Glu Leu Ser Thr Lys Cys Ile Ile Lys
                180                      185                      190

Thr Val Glu Phe Ala Lys Gln Leu Pro Gly Phe Thr Thr Leu Thr Ile
                195                      200                      205

Ala Asp Gln Ile Thr Leu Leu Lys Ala Ala Cys Leu Asp Ile Leu Ile
  210                      215                      220

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Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln Asp Thr Met Thr Phe
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 245 250 255
 Gly Pro Leu Thr Asp Leu Val Phe Ala Phe Ala Asn Gln Leu Leu Pro
 260 265 270
 Leu Glu Met Asp Asp Ala Glu Thr Gly Leu Leu Ser Ala Ile Cys Leu
 275 280 285
 Ile Cys Gly Asp Arg Gln Asp Leu Glu Gln Pro Asp Arg Val Asp Met
 290 295 300
 Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Val Tyr Val Arg Lys Arg
 305 310 315 320
 Arg Pro Ser Arg Pro His Met Phe Pro Lys Met Leu Met Lys Ile Thr
 325 330 335
 Asp Leu Arg Ser Ile Ser Ala Lys Gly Ala Glu Arg Val Ile Thr Leu
 340 345 350
 Lys Met Glu Ile Pro Gly Ser Met Pro Pro Leu Ile Gln Glu Met Leu
 355 360 365
 Glu Asn Ser Glu Gly Leu Asp Thr Leu Ser Gly Gln Pro Gly Gly Gly
 370 375 380
 Gly Arg Asp Gly Gly Gly Leu Ala Pro Pro Pro Gly Ser Cys Ser Pro
 385 390 395 400
 Ser Leu Ser Pro Ser Ser Asn Arg Ser Ser Pro Ala Thr His Ser Pro
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<210> 47

<211> 1284

<212> DNA

<213> Homo sapiens

<400> 47

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ggctgcaagg gcttcttccg ccgcagcatc cagaagaaca tgggtgtacac gtgtcaccgg 240
gacaagaact gcatcatcaa caaggtgacc cggaaccgct gccagtactg ccgactgcag 300
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tcggacgggc tgaccctgaa ccggaccag atgcacaacg ctggcttcgg cccctcacc 780
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<210> 48

<211> 797

<212> PRT

<213> Homo sapiens

<400> 48

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              20              25              30

Arg Gln Pro Ser Pro Ser Pro Ser Pro Thr Glu Arg Ala Pro Ala Ser
      35              40              45

Glu Glu Glu Phe Gln Phe Leu Arg Cys Gln Gln Cys Gln Ala Glu Ala
 50              55              60

Lys Cys Pro Lys Leu Leu Pro Cys Leu His Thr Leu Cys Ser Gly Cys
 65              70              75              80

Leu Glu Ala Ser Gly Met Gln Cys Pro Ile Cys Gln Ala Pro Trp Pro
              85              90              95

Leu Gly Ala Asp Thr Pro Ala Leu Asp Asn Val Phe Phe Glu Ser Leu
      100              105              110

Gln Arg Arg Leu Ser Val Tyr Arg Gln Ile Val Asp Ala Gln Ala Val
      115              120              125

Cys Thr Arg Cys Lys Glu Ser Ala Asp Phe Trp Cys Phe Glu Cys Glu
      130              135              140

Gln Leu Leu Cys Ala Lys Cys Phe Glu Ala His Gln Trp Phe Leu Lys
      145              150              155              160

His Glu Ala Arg Pro Leu Ala Glu Leu Arg Asn Gln Ser Val Arg Glu
              165              170              175

Phe Leu Asp Gly Thr Arg Lys Thr Asn Asn Ile Phe Cys Ser Asn Pro
      180              185              190

Asn His Arg Thr Pro Thr Leu Thr Ser Ile Tyr Cys Arg Gly Cys Ser
      195              200              205

Lys Pro Leu Cys Cys Ser Cys Ala Leu Leu Asp Ser Ser His Ser Glu
      210              215              220

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Leu	Lys	Cys	Asp	Ile	Ser	Ala	Glu	Ile	Gln	Gln	Arg	Gln	Glu	Glu	Leu	225	230	235	240
Asp	Ala	Met	Thr	Gln	Ala	Leu	Gln	Glu	Gln	Asp	Ser	Ala	Phe	Gly	Ala	245	250	255	
Val	His	Ala	Gln	Met	His	Ala	Ala	Val	Gly	Gln	Leu	Gly	Arg	Ala	Arg	260	265	270	
Ala	Glu	Thr	Glu	Glu	Leu	Ile	Arg	Glu	Arg	Val	Arg	Gln	Val	Val	Ala	275	280	285	
His	Val	Arg	Ala	Gln	Glu	Arg	Glu	Leu	Leu	Glu	Ala	Val	Asp	Ala	Arg	290	295	300	
Tyr	Gln	Arg	Asp	Tyr	Glu	Glu	Met	Ala	Ser	Arg	Leu	Gly	Arg	Leu	Asp	305	310	315	320
Ala	Val	Leu	Gln	Arg	Ile	Arg	Thr	Gly	Ser	Ala	Leu	Val	Gln	Arg	Met	325	330	335	
Lys	Cys	Tyr	Ala	Ser	Asp	Gln	Glu	Val	Leu	Asp	Met	His	Gly	Phe	Leu	340	345	350	
Arg	Gln	Ala	Leu	Cys	Arg	Leu	Arg	Gln	Glu	Glu	Pro	Gln	Ser	Leu	Gln	355	360	365	
Ala	Ala	Val	Arg	Thr	Asp	Gly	Phe	Asp	Glu	Phe	Lys	Val	Arg	Leu	Gln	370	375	380	
Asp	Leu	Ser	Ser	Cys	Ile	Thr	Gln	Gly	Lys	Ala	Ile	Glu	Thr	Gln	Ser	385	390	395	400
Ser	Ser	Ser	Glu	Glu	Ile	Val	Pro	Ser	Pro	Pro	Ser	Pro	Pro	Pro	Leu	405	410	415	
Pro	Arg	Ile	Tyr	Lys	Pro	Cys	Phe	Val	Cys	Gln	Asp	Lys	Ser	Ser	Gly	420	425	430	
Tyr	His	Tyr	Gly	Val	Ser	Ala	Cys	Glu	Gly	Cys	Lys	Gly	Phe	Phe	Arg	435	440	445	
Arg	Ser	Ile	Gln	Lys	Asn	Met	Val	Tyr	Thr	Cys	His	Arg	Asp	Lys	Asn	450	455	460	
Cys	Ile	Ile	Asn	Lys	Val	Thr	Arg	Asn	Arg	Cys	Gln	Tyr	Cys	Arg	Leu	465	470	475	480
Gln	Lys	Cys	Phe	Glu	Val	Gly	Met	Ser	Lys	Glu	Ser	Val	Arg	Asn	Asp	485	490	495	
Arg	Asn	Lys	Lys	Lys	Lys	Glu	Val	Pro	Lys	Pro	Glu	Cys	Ser	Glu	Ser	500	505	510	
Tyr	Thr	Leu	Thr	Pro	Glu	Val	Gly	Glu	Leu	Ile	Glu	Lys	Val	Arg	Lys	515	520	525	
Ala	His	Gln	Glu	Thr	Phe	Pro	Ala	Leu	Cys	Gln	Leu	Gly	Lys	Tyr	Thr				

530					535					540					
Thr 545	Asn	Asn	Ser	Ser	Glu 550	Gln	Arg	Val	Ser	Leu 555	Asp	Ile	Asp	Leu	Trp 560
Asp	Lys	Phe	Ser	Glu 565	Leu	Ser	Thr	Lys	Cys 570	Ile	Ile	Lys	Thr	Val 575	Glu
Phe	Ala	Lys	Gln 580	Leu	Pro	Gly	Phe	Thr 585	Thr	Leu	Thr	Ile	Ala 590	Asp	Gln
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Cys	Thr 610	Arg	Tyr	Thr	Pro	Glu 615	Gln	Asp	Thr	Met	Thr 620	Phe	Ser	Asp	Gly
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Asp	Asp	Ala	Glu 660	Thr	Gly	Leu	Leu	Ser 665	Ala	Ile	Cys	Leu	Ile 670	Cys	Gly
Asp	Arg	Gln 675	Asp	Leu	Glu	Gln	Pro 680	Asp	Arg	Val	Asp 685	Met	Leu	Gln	Glu
Pro 690	Leu	Leu	Glu	Ala	Leu	Lys 695	Val	Tyr	Val	Arg	Lys 700	Arg	Arg	Pro	Ser
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Gly 770	Gly	Gly	Leu	Ala	Pro	Pro 775	Pro	Gly	Ser	Cys	Ser 780	Pro	Ser	Leu	Ser
Pro 785	Ser	Ser	Asn	Arg	Ser 790	Ser	Pro	Ala	Thr	His 795	Ser	Pro			

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ttcaagggtg gcctgcagga cctcagctct tgcatcacc aggggaaagc cattgagacc 1260
cagacagca gttctgaaga gatagtcccc agccctccct cgccaccccc tctaccctcg 1320
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gcctgtgagg gctgcaaggg cttcttccgc cgcagcatcc agaagaacat ggtgtacacg 1440
tgtaccggg acaagaactg catcatcaac aaggtgacct ggaaccgctg ccagtactgc 1500
cgactgcaga agtgctttga agtgggcatg tccaaggagt ctgtgagaaa cgaccgaaac 1560
aagaagaaga aggaggtgcc caagcccag tgccttgaga gctacacgct gacgcggag 1620
gtgggggagc tcattgagaa ggtgcgcaaa gcgcaccagg aaaccttccc tgccctctgc 1680
cagctgggca aatacactac gaacaacagc tcagaacaac gtgtctctct ggacattgac 1740
ctctgggaca agttcagtga actctccacc aagtgcacca ttaagactgt ggagttcgcc 1800
aagcagctgc ccggcttcac caccctcacc atcgccgacc agatcacccct cctcaaggct 1860
gcctgcctg acatcctgat cctgcggatc tgcacgcgg acacgcccga gcaggacacc 1920
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ccccccaccg acctggtctt tgcttctgcc aaccagctgc tgcccctgga gatggatgat 2040
gcggagacgg ggctgctcag cgccatctgc ctcatctgcg gagaccgcca ggacctggag 2100
cagccggacc ggggtggacat gctgcaggag ccgctgctgg aggcgctaaa ggtctacgtg 2160
cggaagcgga ggcccagccg cccccacatg tcccccaaga tgctaataga gattactgac 2220
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tgtagcccca gcctcagccc cagctccaac agaagcagcc cggccaccca ctcccgtga 2460
ccgcccacgc cacatggaca cagccctcgc cctccgcccc ggcttttctc tgcccttcta 2520
ccgacctgt gaccccgcac cagccctgcc cccacctgcc ctcccgggca gtactgggga 2580
ccttccctgg gggacgggga gggaggagg agcgactcct tggacagagg cctgggccc 2640
cagtggactg cctgctccca cagcctgggc tgacgtcaga ggccgaggcc aggaactgag 2700
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cctcagaact cacaagccat tgctccccag ctggggaacc tcaacctccc cctgacctg 2880
gttggtgaca gagggggtgg gacaggggag ggggggtccc cctgtacata cctgacctg 2940
ccaaccccag gtattaatc tcgctgggtt tgtttttatt ttaatttttt tgttttgatt 3000
tttttaataa gaattttcat ttttaagcaaa aaaaaa 3036

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<210> 50

<211> 99

<212> PRT

<213> Homo sapiens

<400> 50

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Asp Val Ser Asn Thr Thr Thr Ala Gln Lys Arg Lys Cys Ser Gln Thr
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 Gln Cys Pro Arg Lys Val Ile Lys Met Glu Ser Glu Glu Gly Lys Glu
 20 25 30
 Ala Arg Leu Ala Leu Pro Ala Pro Gly Pro Tyr Ser Thr Pro Leu Arg
 35 40 45
 Thr Pro Leu Trp Asn Gly Ser Asn His Ser Ile Glu Thr Gln Ser Ser
 50 55 60
 Ser Ser Glu Glu Ile Val Pro Ser Pro Pro Ser Pro Pro Pro Leu Pro
 65 70 75 80
 Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys Ser Ser Gly Tyr
 85 90 95
 His Tyr Gly

<210> 51
 <211> 296
 <212> DNA
 <213> Homo sapiens

<400> 51
 gatgtctcca atacaacgac agcccagaag aggaagtgca gccagaccca gtgccccagg 60
 aaggatcatca agatggagtc tgaggagggg aaggaggcaa gggtggctct ccccgccccg 120
 ggtccgtact ccaccccgct ccggactccg ctttggaatg gctcaaacca ctccattgag 180
 acccagagca gcagttctga agagatagtg cccagccctc cctcgccacc cctcttacct 240
 cgcattctaca agccttgctt tgtctgtcag gacaagtcct caggctacca ctatgg 296

<210> 52
 <211> 858
 <212> PRT
 <213> Homo sapiens

<400> 52
 Met Asp Leu Thr Lys Met Gly Met Ile Gln Leu Gln Asn Pro Ser His
 1 5 10 15
 Pro Thr Gly Leu Leu Cys Lys Ala Asn Gln Met Arg Leu Ala Gly Thr
 20 25 30
 Leu Cys Asp Val Val Ile Met Val Asp Ser Gln Glu Phe His Ala His
 35 40 45
 Arg Thr Val Leu Ala Cys Thr Ser Lys Met Phe Glu Ile Leu Phe His
 50 55 60
 Arg Asn Ser Gln His Tyr Thr Leu Asp Phe Leu Ser Pro Lys Thr Phe
 65 70 75 80
 Gln Gln Ile Leu Glu Tyr Ala Tyr Thr Ala Thr Leu Gln Ala Lys Ala
 85 90 95

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Glu Asp Leu Asp Asp Leu Leu Tyr Ala Ala Glu Ile Leu Glu Ile Glu
 100 105 110
 Tyr Leu Glu Glu Gln Cys Leu Lys Met Leu Glu Thr Ile Gln Ala Ser
 115 120 125
 Asp Asp Asn Asp Thr Glu Ala Thr Met Ala Asp Gly Gly Ala Glu Glu
 130 135 140
 Glu Glu Asp Arg Lys Ala Arg Tyr Leu Lys Asn Ile Phe Ile Ser Lys
 145 150 155 160
 His Ser Ser Glu Glu Ser Gly Tyr Ala Ser Val Ala Gly Gln Ser Leu
 165 170 175
 Pro Gly Pro Met Val Asp Gln Ser Pro Ser Val Ser Thr Ser Phe Gly
 180 185 190
 Leu Ser Ala Met Ser Pro Thr Lys Ala Ala Val Asp Ser Leu Met Thr
 195 200 205
 Ile Gly Gln Ser Leu Leu Gln Gly Thr Leu Gln Pro Pro Ala Gly Pro
 210 215 220
 Glu Glu Pro Thr Leu Ala Gly Gly Gly Arg His Pro Gly Val Ala Glu
 225 230 235 240
 Val Lys Thr Glu Met Met Gln Val Asp Glu Val Pro Ser Gln Asp Ser
 245 250 255
 Pro Gly Ala Ala Glu Ser Ser Ile Ser Gly Gly Met Gly Asp Lys Val
 260 265 270
 Glu Glu Arg Gly Lys Glu Gly Pro Gly Thr Pro Thr Arg Ser Ser Val
 275 280 285
 Ile Thr Ser Ala Arg Glu Leu His Tyr Gly Arg Glu Glu Ser Ala Glu
 290 295 300
 Gln Val Pro Pro Pro Ala Glu Ala Gly Gln Ala Pro Thr Gly Arg Pro
 305 310 315 320
 Glu His Pro Ala Pro Pro Pro Glu Lys His Leu Gly Ile Tyr Ser Val
 325 330 335
 Leu Pro Asn His Lys Ala Asp Ala Val Leu Ser Met Pro Ser Ser Val
 340 345 350
 Thr Ser Gly Leu His Val Gln Pro Ala Leu Ala Val Ser Met Asp Phe
 355 360 365
 Ser Thr Tyr Gly Gly Leu Leu Pro Gln Gly Phe Ile Gln Arg Glu Leu
 370 375 380
 Phe Ser Lys Leu Gly Glu Leu Ala Val Gly Met Lys Ser Glu Ser Arg
 385 390 395 400
 Thr Ile Gly Glu Gln Cys Ser Val Cys Gly Val Glu Leu Pro Asp Asn

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405					410					415					
Glu	Ala	Val	Glu	Gln	His	Arg	Lys	Leu	His	Ser	Gly	Met	Lys	Thr	Tyr
			420					425					430		
Gly	Cys	Glu	Leu	Cys	Gly	Lys	Arg	Phe	Leu	Asp	Ser	Leu	Arg	Leu	Arg
		435					440					445			
Met	His	Leu	Leu	Ala	His	Ser	Ala	Ile	Glu	Thr	Gln	Ser	Ser	Ser	Ser
	450					455					460				
Glu	Glu	Ile	Val	Pro	Ser	Pro	Pro	Ser	Pro	Pro	Pro	Leu	Pro	Arg	Ile
465					470					475					480
Tyr	Lys	Pro	Cys	Phe	Val	Cys	Gln	Asp	Lys	Ser	Ser	Gly	Tyr	His	Tyr
				485					490					495	
Gly	Val	Ser	Ala	Cys	Glu	Gly	Cys	Lys	Gly	Phe	Phe	Arg	Arg	Ser	Ile
			500					505					510		
Gln	Lys	Asn	Met	Val	Tyr	Thr	Cys	His	Arg	Asp	Lys	Asn	Cys	Ile	Ile
		515					520					525			
Asn	Lys	Val	Thr	Arg	Asn	Arg	Cys	Gln	Tyr	Cys	Arg	Leu	Gln	Lys	Cys
	530					535					540				
Phe	Glu	Val	Gly	Met	Ser	Lys	Glu	Ser	Val	Arg	Asn	Asp	Arg	Asn	Lys
545					550					555					560
Lys	Lys	Lys	Glu	Val	Pro	Lys	Pro	Glu	Cys	Ser	Glu	Ser	Tyr	Thr	Leu
			565						570					575	
Thr	Pro	Glu	Val	Gly	Glu	Leu	Ile	Glu	Lys	Val	Arg	Lys	Ala	His	Gln
		580						585					590		
Glu	Thr	Phe	Pro	Ala	Leu	Cys	Gln	Leu	Gly	Lys	Tyr	Thr	Thr	Asn	Asn
		595					600					605			
Ser	Ser	Glu	Gln	Arg	Val	Ser	Leu	Asp	Ile	Asp	Leu	Trp	Asp	Lys	Phe
	610					615					620				
Ser	Glu	Leu	Ser	Thr	Lys	Cys	Ile	Ile	Lys	Thr	Val	Glu	Phe	Ala	Lys
625					630					635					640
Gln	Leu	Pro	Gly	Phe	Thr	Thr	Leu	Thr	Ile	Ala	Asp	Gln	Ile	Thr	Leu
			645						650					655	
Leu	Lys	Ala	Ala	Cys	Leu	Asp	Ile	Leu	Ile	Leu	Arg	Ile	Cys	Thr	Arg
		660					665						670		
Tyr	Thr	Pro	Glu	Gln	Asp	Thr	Met	Thr	Phe	Ser	Asp	Gly	Leu	Thr	Leu
		675				680						685			
Asn	Arg	Thr	Gln	Met	His	Met	Ala	Gly	Phe	Gly	Pro	Leu	Thr	Asp	Leu
	690					695					700				
Val	Phe	Ala	Phe	Ala	Asn	Gln	Leu	Leu	Pro	Leu	Glu	Met	Asp	Asp	Ala
705					710					715					720

Glu	Thr	Gly	Leu	Leu	Ser	Ala	Ile	Cys	Leu	Ile	Cys	Gly	Asp	Arg	Gln	
				725					730					735		
Asp	Leu	Glu	Gln	Pro	Asp	Arg	Val	Asp	Met	Leu	Gln	Glu	Pro	Leu	Leu	
				740					745					750		
Glu	Ala	Leu	Lys	Val	Tyr	Val	Arg	Lys	Arg	Arg	Pro	Ser	Arg	Pro	His	
				755					760					765		
Met	Phe	Pro	Lys	Met	Leu	Met	Lys	Ile	Thr	Asp	Leu	Arg	Ser	Ile	Ser	
				770					775					780		
Ala	Lys	Gly	Ala	Glu	Arg	Val	Ile	Thr	Leu	Lys	Met	Glu	Ile	Pro	Gly	
				785					790					795		
Ser	Met	Pro	Pro	Leu	Ile	Gln	Glu	Met	Leu	Glu	Asn	Ser	Glu	Gly	Leu	
				805					810					815		
Asp	Thr	Leu	Ser	Gly	Gln	Pro	Gly	Gly	Gly	Gly	Arg	Asp	Gly	Gly	Gly	
				820					825					830		
Leu	Ala	Pro	Pro	Pro	Gly	Ser	Cys	Ser	Pro	Ser	Leu	Ser	Pro	Ser	Ser	
				835					840					845		
Asn	Arg	Ser	Ser	Pro	Ala	Thr	His	Ser	Pro							
				850					855							

Met	Ala	Ser	Asn	Ser	Ser	Ser	Cys	Pro	Thr	Pro	Gly	Gly	Gly	His	Leu
1				5					10					15	
Asn	Gly	Tyr	Pro	Val	Pro	Pro	Tyr	Ala	Phe	Phe	Phe	Pro	Pro	Met	Leu
			20					25					30		
Gly	Gly	Leu	Ser	Pro	Pro	Gly	Ala	Leu	Thr	Thr	Leu	Gln	His	Gln	Leu
		35					40					45			
Pro	Val	Ser	Gly	Tyr	Ser	Thr	Pro	Ser	Pro	Ala	Thr	Gly	Ala	Lys	Ala
	50					55					60				
Phe	Val	Cys	Asp	Gln	Cys	Gly	Ala	Gln	Phe	Ser	Lys	Glu	Asp	Ala	Leu
65					70				75						80
Glu	Thr	His	Arg	Gln	Thr	His	Thr	Gly	Thr	Asp	Met	Ala	Val	Phe	Cys
				85					90					95	
Leu	Leu	Cys	Gly	Lys	Arg	Phe	Gln	Ala	Gln	Ser	Ala	Leu	Gln	Gln	His
			100					105					110		
Met	Glu	Val	His	Ala	Gly	Val	Arg	Ser	Tyr	Ile	Cys	Ser	Glu	Cys	Asn
		115					120					125			

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Arg Thr Phe Pro Ser His Thr Ala Leu Lys Arg His Leu Arg Ser His
 130 135 140
 Thr Gly Asp His Pro Tyr Glu Cys Glu Phe Cys Gly Ser Cys Phe Arg
 145 150 155 160
 Asp Glu Ser Thr Leu Lys Ser His Lys Arg Ile His Thr Gly Glu Lys
 165 170 175
 Pro Tyr Glu Cys Asn Gly Cys Asp Lys Lys Phe Ser Leu Lys His Gln
 180 185 190
 Leu Glu Thr His Tyr Arg Val His Thr Gly Glu Lys Pro Phe Glu Cys
 195 200 205
 Lys Leu Cys His Gln Arg Ser Arg Asp Tyr Ser Ala Met Ile Lys His
 210 215 220
 Leu Arg Thr His Asn Gly Ala Ser Pro Tyr Gln Cys Thr Ile Cys Thr
 225 230 235 240
 Glu Tyr Cys Pro Ser Leu Ser Ser Met Gln Lys His Met Lys Gly His
 245 250 255
 Lys Pro Glu Glu Ile Pro Pro Asp Trp Arg Ile Glu Lys Thr Tyr Leu
 260 265 270
 Tyr Leu Cys Tyr Val
 275

<210> 54

<211> 2311

<212> PRT

<213> Homo sapiens

<400> 54

Met Ala His Ser Cys Arg Trp Arg Phe Pro Ala Arg Pro Gly Thr Thr
 1 5 10 15
 Gly Gly Gly Gly Gly Gly Gly Arg Arg Gly Leu Gly Gly Gly Pro Arg
 20 25 30
 Gln Arg Val Pro Ala Leu Leu Leu Pro Pro Gly Pro Pro Val Gly Gly
 35 40 45
 Gly Gly Pro Gly Ala Pro Pro Ser Pro Pro Ala Val Ala Ala Ala
 50 55 60
 Ala Ala Ala Gly Ser Ser Gly Ala Gly Val Pro Gly Gly Ala Ala Ala
 65 70 75 80
 Ala Ser Ala Ala Ser Ser Ser Ser Ala Ser Ser Ser Ser Ser Ser
 85 90 95
 Ser Ser Ala Ser Ser Gly Pro Ala Leu Leu Arg Val Gly Pro Gly Phe
 100 105 110

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Asp	Ala	Ala	Leu	Gln	Val	Ser	Ala	Ala	Ile	Gly	Thr	Asn	Leu	Arg	Arg	115	120	125
Phe	Arg	Ala	Val	Phe	Gly	Glu	Ser	Gly	Gly	Gly	Gly	Gly	Ser	Gly	Glu	130	135	140
Leu	Thr	Thr	Gln	Ile	Pro	Cys	Ser	Trp	Arg	Thr	Lys	Gly	His	Ile	His	145	150	155
Asp	Lys	Lys	Thr	Glu	Pro	Phe	Arg	Leu	Leu	Ala	Trp	Ser	Trp	Cys	Leu	165	170	175
Asn	Asp	Glu	Gln	Phe	Leu	Gly	Phe	Gly	Ser	Asp	Glu	Glu	Val	Arg	Val	180	185	190
Arg	Ser	Pro	Thr	Arg	Ser	Pro	Ser	Val	Lys	Thr	Ser	Pro	Arg	Lys	Pro	195	200	205
Arg	Gly	Arg	Pro	Arg	Ser	Gly	Ser	Asp	Arg	Asn	Ser	Ala	Ile	Leu	Ser	210	215	220
Asp	Pro	Ser	Val	Phe	Ser	Pro	Leu	Asn	Lys	Ser	Glu	Thr	Lys	Ser	Gly	225	230	235
Asp	Lys	Ile	Lys	Lys	Lys	Asp	Ser	Lys	Ser	Ile	Glu	Lys	Lys	Arg	Gly	245	250	255
Arg	Pro	Pro	Thr	Phe	Pro	Gly	Val	Lys	Ile	Lys	Ile	Thr	His	Gly	Lys	260	265	270
Asp	Ile	Ser	Glu	Leu	Pro	Lys	Gly	Asn	Lys	Glu	Asp	Ser	Leu	Lys	Lys	275	280	285
Ile	Lys	Arg	Thr	Pro	Ser	Ala	Thr	Phe	Gln	Gln	Ala	Thr	Lys	Ile	Lys	290	295	300
Lys	Leu	Arg	Ala	Gly	Lys	Leu	Ser	Pro	Leu	Lys	Ser	Lys	Phe	Lys	Thr	305	310	315
Gly	Lys	Leu	Gln	Ile	Gly	Arg	Lys	Gly	Val	Gln	Ile	Val	Arg	Arg	Arg	325	330	335
Gly	Arg	Pro	Pro	Ser	Thr	Glu	Arg	Ile	Lys	Thr	Pro	Ser	Gly	Leu	Leu	340	345	350
Ile	Asn	Ser	Glu	Leu	Glu	Lys	Pro	Gln	Lys	Val	Arg	Lys	Asp	Lys	Glu	355	360	365
Gly	Thr	Pro	Pro	Leu	Thr	Lys	Glu	Asp	Lys	Thr	Val	Val	Arg	Gln	Ser	370	375	380
Pro	Arg	Arg	Ile	Lys	Pro	Val	Arg	Ile	Ile	Pro	Ser	Ser	Lys	Arg	Thr	385	390	395
Asp	Ala	Thr	Ile	Ala	Lys	Gln	Leu	Leu	Gln	Arg	Ala	Lys	Lys	Gly	Ala	405	410	415

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Gln Lys Lys Ile Glu Lys Glu Ala Ala Gln Leu Gln Gly Arg Lys Val
 420 425 430
 Lys Thr Gln Val Lys Asn Ile Arg Gln Phe Ile Met Pro Val Val Ser
 435 440 445
 Ala Ile Ser Ser Arg Ile Ile Lys Thr Pro Arg Arg Phe Ile Glu Asp
 450 455 460
 Glu Asp Tyr Asp Pro Pro Ile Lys Ile Ala Arg Leu Glu Ser Thr Pro
 465 470 475 480
 Asn Ser Arg Phe Ser Ala Pro Ser Cys Gly Ser Ser Glu Lys Ser Ser
 485 490 495
 Ala Ala Ser Gln His Ser Ser Gln Met Ser Ser Asp Ser Ser Arg Ser
 500 505 510
 Ser Ser Pro Ser Val Asp Thr Ser Thr Asp Ser Gln Ala Ser Glu Glu
 515 520 525
 Ile Gln Val Leu Pro Glu Glu Arg Ser Asp Thr Pro Glu Val His Pro
 530 535 540
 Pro Leu Pro Ile Ser Gln Ser Pro Glu Asn Glu Ser Asn Asp Arg Arg
 545 550 555 560
 Ser Arg Arg Tyr Ser Val Ser Glu Arg Ser Phe Gly Ser Arg Thr Thr
 565 570 575
 Lys Lys Leu Ser Thr Leu Gln Ser Ala Pro Gln Gln Gln Thr Ser Ser
 580 585 590
 Ser Pro Pro Pro Pro Leu Leu Thr Pro Pro Pro Pro Leu Gln Pro Ala
 595 600 605
 Ser Ser Ile Ser Asp His Thr Pro Trp Leu Met Pro Pro Thr Ile Pro
 610 615 620
 Phe Gly Leu Cys Ser Asn Asn Pro Leu Thr Ser Pro Phe Leu Pro Ala
 625 630 635 640
 Ser Thr Ala Pro Met Gln Gly Lys Arg Lys Ser Ile Leu Arg Glu Pro
 645 650 655
 Thr Phe Arg Trp Thr Ser Leu Lys His Ser Arg Ser Glu Pro Gln Tyr
 660 665 670
 Phe Ser Ser Ala Lys Tyr Ala Lys Glu Gly Leu Ile Arg Lys Pro Ile
 675 680 685
 Phe Asp Asn Phe Arg Pro Pro Pro Leu Thr Pro Glu Asp Val Gly Phe
 690 695 700
 Ala Ser Gly Phe Ser Ala Ser Gly Thr Ala Ala Ser Ala Arg Leu Phe
 705 710 715 720
 Ser Pro Leu His Ser Gly Thr Arg Phe Asp Met His Lys Arg Ser Pro

735

Leu	Leu	Arg	Ala	Pro	Arg	Phe	Thr	Pro	Ser	Glu	Ala	His	Ser	Arg	Ile	
			740							745				750		
Phe	Glu	Ser	Val	Thr	Leu	Pro	Ser	Asn	Arg	Thr	Ser	Ala	Gly	Thr	Ser	
			755							760				765		
Ser	Ser	Gly	Val	Ser	Asn	Arg	Lys	Arg	Lys	Arg	Lys	Val	Phe	Ser	Pro	
			770							775				780		
Ile	Arg	Ser	Glu	Pro	Arg	Ser	Pro	Ser	His	Ser	Met	Arg	Thr	Arg	Ser	
			785							790				795		
Gly	Arg	Leu	Ser	Ser	Ser	Glu	Leu	Ser	Pro	Leu	Thr	Pro	Pro	Ser	Ser	
			805							810				815		
Val	Ser	Ser	Ser	Leu	Ser	Ile	Ser	Val	Ser	Pro	Leu	Ala	Thr	Ser	Ala	
			820							825				830		
Leu	Asn	Pro	Thr	Phe	Thr	Phe	Pro	Ser	His	Ser	Leu	Thr	Gln	Ser	Gly	
			835							840				845		
Glu	Ser	Ala	Glu	Lys	Asn	Gln	Arg	Pro	Arg	Lys	Gln	Thr	Ser	Ala	Pro	
			850							855				860		
Ala	Glu	Pro	Phe	Ser	Ser	Ser	Ser	Pro	Thr	Pro	Leu	Phe	Pro	Trp	Phe	
			865							870				875		
Thr	Pro	Gly	Ser	Gln	Thr	Glu	Arg	Gly	Arg	Asn	Lys	Asp	Lys	Ala	Pro	
			885							890				895		
Glu	Glu	Leu	Ser	Lys	Asp	Arg	Asp	Ala	Asp	Lys	Ser	Val	Glu	Lys	Asp	
			900							905				910		
Lys	Ser	Arg	Glu	Arg	Asp	Arg	Glu	Arg	Glu	Lys	Glu	Asn	Lys	Arg	Glu	
			915							920				925		
Ser	Arg	Lys	Glu	Lys	Arg	Lys	Lys	Gly	Ser	Glu	Ile	Gln	Ser	Ser	Ser	
			930							935				940		
Ala	Leu	Tyr	Pro	Val	Gly	Arg	Val	Ser	Lys	Glu	Lys	Val	Val	Gly	Glu	
			945							950				955		
Asp	Val	Ala	Thr	Ser	Ser	Ser	Ala	Lys	Lys	Ala	Thr	Gly	Arg	Lys	Lys	
			965							970				975		
Ser	Ser	Ser	His	Asp	Ser	Gly	Thr	Asp	Ile	Thr	Ser	Val	Thr	Leu	Gly	
			980							985				990		
Asp	Thr	Thr	Ala	Val	Lys	Thr	Lys	Ile	Leu	Ile	Lys	Lys	Gly	Arg	Gly	
			995							1000				1005		
Asn	Leu	Glu	Lys	Thr	Asn	Leu	Asp	Leu	Gly	Pro	Thr	Ala	Pro	Ser	Leu	
			1010							1015				1020		
Glu	Lys	Glu	Lys	Thr	Leu	Cys	Leu	Ser	Thr	Pro	Ser	Ser	Ser	Thr	Val	
			1025							1030				1035		

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Lys His Ser Thr Ser Ser Ile Gly Ser Met Leu Ala Gln Ala Asp Lys
 1045 1050 1055
 Leu Pro Met Thr Asp Lys Arg Val Ala Ser Leu Leu Lys Lys Ala Lys
 1060 1065 1070
 Ala Gln Leu Cys Lys Ile Glu Lys Ser Lys Ser Leu Lys Gln Thr Asp
 1075 1080 1085
 Gln Pro Lys Ala Gln Gly Gln Glu Ser Asp Ser Ser Glu Thr Ser Val
 1090 1095 1100
 Arg Gly Pro Arg Ile Lys His Val Cys Arg Arg Ala Ala Val Ala Leu
 1105 1110 1115 1120
 Gly Arg Lys Arg Ala Val Phe Pro Asp Asp Met Pro Thr Leu Ser Ala
 1125 1130 1135
 Leu Pro Trp Glu Glu Arg Glu Lys Ile Leu Phe Ser Met Gly Asn Asp
 1140 1145 1150
 Asp Lys Ser Ser Ile Ala Gly Ser Glu Asp Ala Glu Pro Leu Ala Pro
 1155 1160 1165
 Pro Ile Lys Pro Ile Lys Pro Val Thr Arg Asn Lys Ala Pro Gln Glu
 1170 1175 1180
 Pro Pro Val Lys Lys Gly Arg Arg Ser Arg Arg Cys Gly Gln Cys Pro
 1185 1190 1195 1200
 Gly Cys Gln Val Pro Glu Asp Cys Gly Val Cys Thr Asn Cys Leu Asp
 1205 1210 1215
 Lys Pro Lys Phe Gly Gly Arg Asn Ile Lys Lys Gln Cys Cys Lys Met
 1220 1225 1230
 Arg Lys Cys Gln Asn Leu Gln Trp Met Pro Ser Lys Ala Tyr Leu Gln
 1235 1240 1245
 Lys Gln Ala Lys Ala Val Lys Lys Lys Glu Lys Lys Ser Lys Thr Ser
 1250 1255 1260
 Glu Lys Lys Asp Ser Lys Glu Ser Ser Val Val Lys Asn Val Val Asp
 1265 1270 1275 1280
 Ser Ser Gln Lys Pro Thr Pro Ser Ala Arg Glu Asp Pro Ala Pro Lys
 1285 1290 1295
 Lys Ser Ser Ser Glu Pro Pro Pro Arg Lys Pro Val Glu Glu Lys Ser
 1300 1305 1310
 Glu Glu Gly Asn Val Ser Ala Pro Gly Pro Glu Ser Lys Gln Ala Thr
 1315 1320 1325
 Thr Pro Ala Ser Arg Lys Ser Ser Lys Gln Val Ser Gln Pro Ala Leu
 1330 1335 1340

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Val Ile Pro Pro Gln Pro Pro Thr Thr Gly Pro Pro Arg Lys Glu Val
 1345 1350 1355 1360
 Pro Lys Thr Thr Pro Ser Glu Pro Lys Lys Lys Gln Pro Pro Pro Pro
 1365 1370 1375
 Glu Ser Gly Pro Glu Gln Ser Lys Gln Lys Lys Val Ala Pro Arg Pro
 1380 1385 1390
 Ser Ile Pro Val Lys Gln Lys Pro Lys Glu Lys Glu Lys Pro Pro Pro
 1395 1400 1405
 Val Asn Lys Gln Glu Asn Ala Gly Thr Leu Asn Ile Phe Ser Thr Leu
 1410 1415 1420
 Ser Asn Gly Asn Ser Ser Lys Gln Lys Ile Pro Ala Asp Gly Val His
 1425 1430 1435 1440
 Arg Ile Arg Val Asp Phe Lys Gln Thr Tyr Ser Asn Glu Val His Cys
 1445 1450 1455
 Val Glu Glu Ile Leu Lys Glu Met Thr His Ser Trp Pro Pro Pro Leu
 1460 1465 1470
 Thr Ala Ile His Thr Pro Ser Thr Ala Glu Pro Ser Lys Phe Pro Phe
 1475 1480 1485
 Pro Thr Lys Asp Ser Gln His Val Ser Ser Val Thr Gln Asn Gln Lys
 1490 1495 1500
 Gln Tyr Asp Thr Ser Ser Lys Thr His Ser Asn Ser Gln Gln Gly Thr
 1505 1510 1515 1520
 Ser Ser Met Leu Glu Asp Asp Leu Gln Leu Ser Asp Ser Glu Asp Ser
 1525 1530 1535
 Asp Ser Glu Gln Thr Pro Glu Lys Pro Pro Ser Ser Ser Ala Pro Pro
 1540 1545 1550
 Ser Ala Pro Gln Ser Leu Pro Glu Pro Val Ala Ser Ala His Ser Ser
 1555 1560 1565
 Ser Ala Glu Ser Glu Ser Thr Ser Asp Ser Asp Ser Ser Ser Asp Ser
 1570 1575 1580
 Glu Ser Glu Ser Ser Ser Asp Ser Glu Glu Asn Glu Pro Leu Glu
 1585 1590 1595 1600
 Thr Pro Ala Pro Glu Pro Glu Pro Pro Thr Thr Asn Lys Trp Gln Leu
 1605 1610 1615
 Asp Asn Trp Leu Thr Lys Val Ser Ser Gln Leu Arg His Gln Arg Ala
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 Pro Gly Ala Gln Ser Pro His Gly Gly Thr Gln Arg Val Arg Ala Ala
 1635 1640 1645
 Ala Thr Val Pro Arg Val Arg Ser Ile Leu Asn Pro Lys Ile Leu Pro

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Gly Lys Arg Ser Cys Gln Lys Ser Pro Ala Gln Gln Glu Pro Pro Gln		
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	1730	1735 1740
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Pro Ala Val Pro Pro Ser Ser Glu Lys Lys Lys His Lys Ser Ser Leu		
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	1780	1785 1790
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Ser Gln Gly Pro Pro His Ser Gly Ser Ser Ser Arg Thr Ser Gly Cys		
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Pro Pro Gln Ser Leu Met Val Lys Ile Thr Leu Asp Leu Leu Ser Arg		
	1860	1865 1870
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Asp Ser Ser Ser Lys Leu Ala Lys Lys Arg Lys Gly Glu Ala Glu Arg		
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Asp Cys Asp Asn Lys Lys Ile Arg Leu Glu Lys Glu Ile Lys Ser Gln		
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	1955	1960 1965

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 2005 2010 2015
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 2020 2025 2030
 Ser Gly Asp Thr Ala Asn Pro Phe Pro Val Pro Ser Leu Pro Asn Gly
 2035 2040 2045
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 2050 2055 2060
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Phe Phe Ala Arg Leu Ser Thr Asn Val Cys Thr Leu Ala Leu Asn Ser
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<212> DNA

<213> Homo sapiens

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<211> 277

<212> PRT

<213> Homo sapiens

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Val Ser Gln Pro Ala Leu Val Ile Pro Pro Gln Pro Pro Thr Thr Gly
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Pro Pro Arg Lys Glu Val Pro Lys Thr Thr Pro Ser Glu Pro Lys Lys
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Lys Gln Pro Pro Pro Pro Glu Ser Gly Pro Glu Gln Ser Lys Gln Lys
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Lys Val Ala Pro Arg Pro Ser Ile Pro Val Lys Gln Lys Pro Lys Glu
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Lys Glu Lys Pro Pro Pro Val Asn Lys Gln Glu Asn Ala Gly Thr Leu
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Asn Ile Phe Ser Thr Leu Ser Asn Gly Asn Ser Ser Lys Gln Lys Ile
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Pro Ala Asp Gly Val His Arg Ile Arg Val Asp Phe Lys Glu Asp Cys
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Glu Ala Glu Asn Val Trp Glu Met Gly Gly Leu Gly Ile Leu Thr Ser
      165             170             175

Val Pro Ile Thr Pro Arg Val Val Cys Phe Leu Cys Ala Ser Ser Gly

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Pro Ser Thr Ala Glu Pro Ser Lys Phe Pro Phe Pro Thr Lys Asp Ser		
225	230	235
Gln His Val Ser Ser Val Thr Gln Asn Gln Lys Gln Tyr Asp Thr Ser		
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Gln Lys Ile Pro Ala Asp Gly Val His Arg Ile Arg Val Asp Phe Lys
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<210> 61

<211> 741

<212> DNA

<213> Homo sapiens

<400> 61

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<211> 149

<212> PRT

<213> Homo sapiens

<400> 64

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Ile His Thr Pro Ser Thr Ala Glu Pro Ser Lys Phe Pro Phe Pro Thr
      35              40              45

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```

Lys Asp Ser Gln His Val Ser Ser Val Thr Gln Asn Gln Lys Gln Tyr
      50              55              60

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Asp Thr Ser Ser Lys Thr His Ser Asn Ser Gln Gln Gly Thr Ser Ser
      65              70              75              80

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```

Met Leu Glu Asp Asp Leu Gln Leu Ser Asp Ser Glu Asp Ser Asp Ser
      85              90              95

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Glu Gln Thr Pro Glu Lys Pro Pro Ser Ser Ala Pro Pro Ser Ala
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Pro Gln Ser Leu Pro Glu Pro Val Ala Ser Ala His Ser Ser Ser Ala
      115              120              125

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Glu Ser Glu Ser Thr Ser Asp Ser Asp Ser Ser Asp Ser Glu Ser
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Glu Ser Ser Ser Ser
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<211> 450
<212> DNA
<213> Homo sapiens

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<210> 66
<211> 149
<212> PRT
<213> Homo sapiens

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35 40 45
Lys Asp Ser Gln His Val Ser Ser Val Thr Gln Asn Gln Lys Gln Tyr
50 55 60
Asp Thr Ser Ser Lys Thr His Ser Asn Ser Gln Gln Gly Thr Ser Ser
65 70 75 80
Met Leu Glu Asp Asp Leu Gln Leu Ser Asp Ser Glu Asp Ser Asp Ser
85 90 95
Glu Gln Thr Pro Glu Lys Pro Pro Ser Ser Ser Ala Pro Pro Ser Ala
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Glu Ser Glu Ser Thr Ser Asp Ser Asp Ser Ser Ser Asp Ser Glu Ser
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<210> 67
<211> 450
<212> DNA
<213> Homo sapiens

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<400> 67

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<211> 198

<212> PRT

<213> Homo sapiens

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Ser Asn Asn Ser Lys Gly Tyr Cys Pro Ala Lys Ser Pro Lys Asp Leu
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Ala Val Lys Val His Asp Lys Glu Thr Pro Gln Asp Ser Leu Val Ala
      50              55              60

Pro Ala Gln Pro Pro Ser Gln Thr Phe Pro Pro Pro Ser Leu Pro Ser
      65              70              75              80

Lys Ser Val Ala Met Gln Gln Lys Pro Thr Ala Tyr Val Arg Pro Met
      85              90              95

Asp Gly Gln Asp Gln Ala Pro Ser Glu Ser Pro Glu Leu Lys Pro Leu
      100              105              110

Pro Glu Asp Tyr Arg Gln Gln Thr Phe Glu Lys Thr Asp Leu Lys Val
      115              120              125

Pro Ala Lys Ala Lys Leu Thr Lys Leu Lys Met Pro Ser Gln Ser Val
      130              135              140

Glu Gln Thr Tyr Ser Asn Glu Val His Cys Val Glu Glu Ile Leu Lys
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Glu Lys Pro Pro Pro Val Asn Lys Gln Glu Asn Ala Gly Thr Leu Asn
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Ala Asp Gly Val His Arg
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 gaaaaaccac ctccggtcaa taagcaggag aatgcaggca ctttgaacat cctcagcact 540
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<210> 71
 <211> 198
 <212> PRT
 <213> Homo sapiens

<400> 71
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 35 40 45
 Ala Val Lys Val His Asp Lys Glu Thr Pro Gln Asp Ser Leu Val Ala
 50 55 60
 Pro Ala Gln Pro Pro Ser Gln Thr Phe Pro Pro Pro Ser Leu Pro Ser
 65 70 75 80
 Lys Ser Val Ala Met Gln Gln Lys Pro Thr Ala Tyr Val Arg Pro Met
 85 90 95
 Asp Gly Gln Asp Gln Ala Pro Ser Glu Ser Pro Glu Leu Lys Pro Leu
 100 105 110
 Pro Glu Asp Tyr Arg Gln Gln Thr Phe Glu Lys Thr Asp Leu Lys Val
 115 120 125
 Pro Ala Lys Ala Lys Leu Thr Lys Leu Lys Met Pro Ser Gln Ser Val
 130 135 140

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Glu Gln Thr Tyr Ser Asn Glu Val His Cys Val Glu Glu Ile Leu Lys
 145 150 155 160

Glu Lys Pro Pro Pro Val Asn Lys Gln Glu Asn Ala Gly Thr Leu Asn
 165 170 175

Ile Leu Ser Thr Leu Ser Asn Gly Asn Ser Ser Lys Gln Lys Ile Pro
 180 185 190

Ala Asp Gly Val His Arg
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<210> 72
 <211> 596
 <212> DNA
 <213> Homo sapiens

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<210> 73
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 <212> DNA
 <213> Homo sapiens

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<210> 74
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 <212> DNA
 <213> Homo sapiens

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<400> 74

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<210> 75

<211> 60

<212> DNA

<213> Homo sapiens

<400> 75

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<210> 76

<211> 74

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<212> DNA

<213> Homo sapiens

<400> 76

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<212> DNA

<213> Homo sapiens

<400> 77

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<210> 78

<211> 501

<212> PRT

<213> Homo sapiens

<400> 78

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 20 25 30

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 35 40 45

Asp Leu Gly Glu Lys Val His Thr Glu Gly Arg Ser Glu Pro Ile Leu
 50 55 60

Leu Pro Ser Arg Leu Ser Glu Pro Ala Gly Gly Pro Gln Pro Gly Ile
 65 70 75 80

Leu Gly Ala Val Thr Gly Pro Arg Lys Gly Gly Ser Arg Arg Asn Ala
 85 90 95

Trp Gly Asn Gln Ser Tyr Ala Glu Phe Ile Ser Gln Ala Ile Glu Ser
 100 105 110

Ala Pro Glu Lys Arg Leu Thr Leu Ala Gln Ile Tyr Glu Trp Met Val
 115 120 125

Arg Thr Val Pro Tyr Phe Lys Asp Lys Gly Asp Ser Asn Ser Ser Ala
 130 135 140

Gly Trp Lys Asn Ser Ile Arg His Asn Leu Ser Leu His Ser Lys Phe
 145 150 155 160

Ile Lys Val His Asn Glu Ala Thr Gly Lys Ser Ser Trp Trp Met Leu
 165 170 175

Asn Pro Glu Gly Gly Lys Ser Gly Lys Ala Pro Arg Arg Arg Ala Ala

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180					185					190					
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Glu	Ser	Glu	Val	Leu	Ala	Glu	Glu	Ile	Pro	Ala	Ser	Val	Ser	Ser	Tyr
		275					280					285			
Ala	Gly	Gly	Val	Pro	Pro	Thr	Leu	Asn	Glu	Gly	Leu	Glu	Leu	Leu	Asp
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Gly	Leu	Asn	Leu	Thr	Ser	Ser	His	Ser	Leu	Leu	Ser	Arg	Ser	Gly	Leu
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Ser	Gly	Phe	Ser	Leu	Gln	His	Pro	Gly	Val	Thr	Gly	Pro	Leu	His	Thr
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		355					360					365			
Asp	Thr	Pro	Pro	Pro	Pro	Ala	Asp	Val	Leu	Met	Thr	Gln	Val	Asp	Pro
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Ser	Ser	Lys	Leu	Ala	Thr	Gly	Val	Gly	Leu	Cys	Pro	Lys	Pro	Leu	Glu
				405					410					415	
Ala	Arg	Gly	Pro	Ser	Ser	Leu	Val	Pro	Thr	Leu	Ser	Met	Ile	Ala	Pro
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Pro	Pro	Val	Met	Ala	Ser	Ala	Pro	Ile	Pro	Lys	Ala	Leu	Gly	Thr	Pro
		435					440					445			
Val	Leu	Thr	Pro	Pro	Thr	Glu	Ala	Ala	Ser	Gln	Asp	Arg	Met	Pro	Gln
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Asp	Leu	Asp	Leu	Asp	Met	Tyr	Met	Glu	Asn	Leu	Glu	Cys	Asp	Met	Asp
465					470					475					480
Asn	Ile	Ile	Ser	Asp	Leu	Met	Asp	Glu	Gly	Glu	Gly	Leu	Asp	Phe	Asn
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Phe Glu Pro Asp Pro
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<210> 79

<211> 3171

<212> DNA

<213> Homo sapiens

<400> 79

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<210> 80

<211> 501

<212> PRT

<213> Homo sapiens

<400> 80

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Asp Leu Gly Glu Lys Val His Thr Glu Gly Arg Ser Glu Pro Ile Leu
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Leu Pro Ser Arg Leu Ser Glu Pro Ala Gly Gly Pro Gln Pro Gly Ile
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Leu Gly Ala Val Thr Gly Pro Arg Lys Gly Gly Ser Arg Arg Asn Ala
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Trp Gly Asn Gln Ser Tyr Ala Glu Phe Ile Ser Gln Ala Ile Glu Ser
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Ala Pro Glu Lys Arg Leu Thr Leu Ala Gln Ile Tyr Glu Trp Met Val
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Arg Thr Val Pro Tyr Phe Lys Asp Lys Gly Asp Ser Asn Ser Ser Ala
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Gly Trp Lys Asn Ser Ile Arg His Asn Leu Ser Leu His Ser Lys Phe
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Ile Lys Val His Asn Glu Ala Thr Gly Lys Ser Ser Trp Trp Met Leu
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Asn Pro Glu Gly Gly Lys Ser Gly Lys Ala Pro Arg Arg Arg Ala Ala
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Ser Met Asp Ser Ser Ser Lys Leu Leu Arg Gly Arg Ser Lys Ala Pro
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Thr Ser Pro Val Gly His Phe Ala Lys Trp Ser Gly Ser Pro Cys Ser
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 Glu Gly Cys Phe Ser Ser Ser Gln Ala Leu Glu Ala Leu Leu Thr Ser
 355 360 365
 Asp Thr Pro Pro Pro Pro Ala Asp Val Leu Met Thr Gln Val Asp Pro
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 Ile Leu Ser Gln Ala Pro Thr Leu Leu Leu Leu Gly Gly Leu Pro Ser
 385 390 395 400
 Ser Ser Lys Leu Ala Thr Gly Val Gly Leu Cys Pro Lys Pro Leu Glu
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 Ala Arg Gly Pro Ser Ser Leu Val Pro Thr Leu Ser Met Ile Ala Pro
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 Pro Pro Val Met Ala Ser Ala Pro Ile Pro Lys Ala Leu Gly Thr Pro
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 Asp Leu Asp Leu Asp Met Tyr Met Glu Asn Leu Glu Cys Asp Met Asp
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 Phe Glu Pro Asp Pro
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<210> 81

<211> 3171

<212> DNA

<213> Homo sapiens

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<400> 81

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<210> 82

<211> 74

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<212> DNA

<213> Homo sapiens

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<210> 83

<211> 22

<212> PRT

<213> Homo sapiens

<400> 83

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<210> 84

<211> 69

<212> DNA

<213> Homo sapiens

<400> 84

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<210> 85

<211> 23

<212> PRT

<213> Homo sapiens

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<211> 69

<212> DNA

<213> Homo sapiens

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caagataaa 69

<210> 87

<211> 23

<212> PRT

<213> Homo sapiens

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<400> 87

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1 5 10 15

Arg Phe Tyr Phe Gln Asp Lys
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<210> 88

<211> 69

<212> DNA

<213> Homo sapiens

<400> 88

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caagataaa 69

<210> 89

<211> 76

<212> PRT

<213> Homo sapiens

<400> 89

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Thr Ser Asn Lys Asp Pro Ile Ser His Ser Gly Gly Met Leu Arg Ala
35 40 45

Val Cys Ser Thr Pro Leu Ser Ser Ser Leu Leu Gly Pro Pro Gly Thr
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Ser Ala Leu Pro Arg Leu Ser Arg Ser Pro Phe Thr
65 70 75

<210> 90

<211> 228

<212> DNA

<213> Homo sapiens

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cacagtggcg ggatgctgcg ggctgtctgc agcaccctc tctcctccag cctcctgggg 180
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<210> 91

<211> 1093

<212> PRT

<213> Homo sapiens

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<400> 91

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			20					25					30		
Ala	Val	His	Gln	Ala	Cys	Tyr	Gly	Ile	Val	Gln	Val	Pro	Thr	Gly	Pro
		35					40					45			
Trp	Phe	Cys	Arg	Lys	Cys	Glu	Ser	Gln	Glu	Arg	Ala	Ala	Arg	Val	Arg
	50					55					60				
Cys	Glu	Leu	Cys	Pro	His	Lys	Asp	Gly	Ala	Leu	Lys	Arg	Thr	Asp	Asn
65					70					75					80
Gly	Gly	Trp	Ala	His	Val	Val	Cys	Ala	Leu	Tyr	Ile	Pro	Glu	Val	Gln
				85					90					95	
Phe	Ala	Asn	Val	Leu	Thr	Met	Glu	Pro	Ile	Val	Leu	Gln	Tyr	Val	Pro
			100					105					110		
His	Asp	Arg	Phe	Asn	Lys	Thr	Cys	Tyr	Ile	Cys	Glu	Glu	Thr	Gly	Arg
		115					120					125			
Glu	Ser	Lys	Ala	Ala	Ser	Gly	Ala	Cys	Met	Thr	Cys	Asn	Arg	His	Gly
	130					135					140				
Cys	Arg	Gln	Ala	Phe	His	Val	Thr	Cys	Ala	Gln	Met	Ala	Gly	Leu	Leu
145					150					155					160
Cys	Glu	Glu	Glu	Val	Leu	Glu	Val	Asp	Asn	Val	Lys	Tyr	Cys	Gly	Tyr
				165					170					175	
Cys	Lys	Tyr	His	Phe	Ser	Lys	Met	Lys	Thr	Ser	Arg	His	Ser	Ser	Gly
			180					185					190		
Gly	Gly	Gly	Gly	Gly	Ala	Gly	Gly	Gly	Gly	Gly	Ser	Met	Gly	Gly	Gly
		195				200						205			
Gly	Ser	Gly	Phe	Ile	Ser	Gly	Arg	Arg	Ser	Arg	Ser	Ala	Ser	Pro	Ser
	210					215					220				
Thr	Gln	Gln	Glu	Lys	His	Pro	Thr	His	His	Glu	Arg	Gly	Gln	Lys	Lys
225					230					235					240
Ser	Arg	Lys	Asp	Lys	Glu	Arg	Leu	Lys	Gln	Lys	His	Lys	Lys	Arg	Pro
				245					250					255	
Glu	Ser	Pro	Pro	Ser	Ile	Leu	Thr	Pro	Pro	Val	Val	Pro	Thr	Ala	Asp
			260					265					270		
Lys	Val	Ser	Ser	Ser	Ala	Ser	Ser	Ser	Ser	His	His	Glu	Ala	Ser	Thr
		275					280					285			
Gln	Glu	Thr	Ser	Glu	Ser	Ser	Arg	Glu	Ser	Lys	Gly	Lys	Lys	Ser	Ser
	290					295					300				

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Ser His Ser Leu Ser His Lys Gly Lys Lys Leu Ser Ser Gly Lys Gly
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 Val Ser Ser Phe Thr Ser Ala Ser Ser Ser Ser Ser Ser Ser Ser
 325 330 335
 Ser Ser Gly Gly Pro Phe Gln Pro Ala Val Ser Ser Leu Gln Ser Ser
 340 345 350
 Pro Asp Phe Ser Ala Phe Pro Lys Leu Glu Gln Pro Glu Glu Asp Lys
 355 360 365
 Tyr Ser Lys Pro Thr Ala Pro Ala Pro Ser Ala Pro Pro Ser Pro Ser
 370 375 380
 Ala Pro Glu Pro Pro Lys Ala Asp Leu Phe Glu Gln Lys Val Val Phe
 385 390 395 400
 Ser Gly Phe Gly Pro Ile Met Arg Phe Ser Thr Thr Thr Ser Ser Ser
 405 410 415
 Gly Arg Ala Arg Ala Pro Ser Pro Gly Asp Tyr Lys Ser Pro His Val
 420 425 430
 Thr Gly Ser Gly Ala Ser Ala Gly Thr His Lys Arg Met Pro Ala Leu
 435 440 445
 Ser Ala Thr Pro Val Pro Ala Asp Glu Thr Pro Glu Thr Gly Leu Lys
 450 455 460
 Glu Lys Lys His Lys Ala Ser Lys Arg Ser Arg His Gly Pro Gly Arg
 465 470 475 480
 Pro Lys Gly Ser Arg Asn Lys Glu Gly Thr Gly Gly Pro Ala Ala Pro
 485 490 495
 Ser Leu Pro Ser Ala Gln Leu Ala Gly Phe Thr Ala Thr Ala Ala Ser
 500 505 510
 Pro Phe Ser Gly Gly Ser Leu Val Ser Ser Gly Leu Gly Gly Leu Ser
 515 520 525
 Ser Arg Thr Phe Gly Pro Ser Gly Ser Leu Pro Ser Leu Ser Leu Glu
 530 535 540
 Ser Pro Leu Leu Gly Ala Gly Ile Tyr Thr Ser Asn Lys Asp Pro Ile
 545 550 555 560
 Ser His Ser Gly Gly Met Leu Arg Ala Val Cys Ser Thr Pro Leu Ser
 565 570 575
 Ser Ser Leu Leu Gly Pro Pro Gly Thr Ser Ala Leu Pro Arg Leu Ser
 580 585 590
 Arg Ser Pro Phe Thr Ser Thr Leu Pro Ser Ser Ser Ala Ser Ile Ser
 595 600 605
 Thr Thr Gln Val Phe Ser Leu Ala Gly Ser Thr Phe Ser Leu Pro Ser

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610					615					620					
Thr	His	Ile	Phe	Gly	Thr	Pro	Met	Gly	Ala	Val	Asn	Pro	Leu	Leu	Ser
625					630					635					640
Gln	Ala	Glu	Ser	Ser	His	Thr	Glu	Pro	Asp	Leu	Glu	Asp	Cys	Ser	Phe
				645					650					655	
Arg	Cys	Arg	Gly	Thr	Ser	Pro	Gln	Glu	Ser	Leu	Ser	Ser	Met	Ser	Pro
			660					665					670		
Ile	Ser	Ser	Leu	Pro	Ala	Leu	Phe	Asp	Gln	Thr	Ala	Ser	Ala	Pro	Cys
			675				680					685			
Gly	Gly	Gly	Gln	Leu	Asp	Pro	Ala	Ala	Pro	Gly	Thr	Thr	Asn	Met	Glu
			690			695					700				
Gln	Leu	Leu	Glu	Lys	Gln	Gly	Asp	Gly	Glu	Ala	Gly	Val	Asn	Ile	Val
705					710					715					720
Glu	Met	Leu	Lys	Ala	Leu	His	Ala	Leu	Gln	Lys	Glu	Asn	Gln	Arg	Leu
				725					730					735	
Gln	Glu	Gln	Ile	Leu	Ser	Leu	Thr	Ala	Lys	Lys	Glu	Arg	Leu	Gln	Ile
			740					745					750		
Leu	Asn	Val	Gln	Leu	Ser	Val	Pro	Phe	Pro	Ala	Leu	Pro	Ala	Ala	Leu
			755				760					765			
Pro	Ala	Ala	Asn	Gly	Pro	Val	Pro	Gly	Pro	Tyr	Gly	Leu	Pro	Pro	Gln
			770			775					780				
Ala	Gly	Ser	Ser	Asp	Ser	Leu	Ser	Thr	Ser	Lys	Ser	Pro	Pro	Gly	Lys
785					790					795					800
Ser	Ser	Leu	Gly	Leu	Asp	Asn	Ser	Leu	Ser	Thr	Ser	Ser	Glu	Asp	Pro
				805					810					815	
His	Ser	Gly	Cys	Pro	Ser	Arg	Ser	Ser	Ser	Ser	Leu	Ser	Phe	His	Ser
			820					825					830		
Thr	Pro	Pro	Pro	Leu	Pro	Leu	Leu	Gln	Gln	Ser	Pro	Ala	Thr	Leu	Pro
				835			840					845			
Leu	Ala	Leu	Pro	Gly	Ala	Pro	Ala	Pro	Leu	Pro	Pro	Gln	Pro	Gln	Asn
				850		855					860				
Gly	Leu	Gly	Arg	Ala	Pro	Gly	Ala	Ala	Gly	Leu	Gly	Ala	Met	Pro	Met
865					870					875					880
Ala	Glu	Gly	Leu	Leu	Gly	Gly	Leu	Ala	Gly	Ser	Gly	Gly	Leu	Pro	Leu
				885					890					895	
Asn	Gly	Leu	Leu	Gly	Gly	Leu	Asn	Gly	Ala	Ala	Ala	Pro	Asn	Pro	Ala
			900				905						910		
Ser	Leu	Ser	Gln	Ala	Gly	Gly	Ala	Pro	Thr	Leu	Gln	Leu	Pro	Gly	Cys
			915				920					925			

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Leu Asn Ser Leu Thr Glu Gln Gln Arg His Leu Leu Gln Gln Gln Glu
 930 935 940
 Gln Gln Leu Gln Gln Leu Gln Gln Leu Leu Ala Ser Pro Gln Leu Thr
 945 950 955 960
 Pro Glu His Gln Thr Val Val Tyr Gln Met Ile Gln Gln Ile Gln Gln
 965 970 975
 Lys Arg Glu Leu Gln Arg Leu Gln Met Ala Gly Gly Ser Gln Leu Pro
 980 985 990
 Met Ala Ser Leu Leu Ala Gly Ser Ser Thr Pro Leu Leu Ser Ala Gly
 995 1000 1005
 Thr Pro Gly Leu Leu Pro Thr Ala Ser Ala Pro Pro Leu Leu Pro Ala
 1010 1015 1020
 Gly Ala Leu Val Ala Pro Ser Leu Gly Asn Asn Thr Ser Leu Met Ala
 1025 1030 1035 1040
 Ala Ala Ala Ala Ala Ala Ala Val Ala Ala Ala Gly Gly Pro Pro Val
 1045 1050 1055
 Leu Thr Ala Gln Thr Asn Pro Phe Leu Ser Leu Ser Gly Ala Glu Gly
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 Ser Gly Gly Gly Pro Lys Gly Gly Thr Ala Asp Lys Gly Ala Ser Ala
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 Asn Gln Glu Lys Gly
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<210> 92

<211> 3282

<212> DNA

<213> Homo sapiens

<400> 92

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<210> 93

<211> 752

<212> PRT

<213> Homo sapiens

<400> 93

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      20              25              30

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Ala Pro Asp Ala Gly Ala Ala Leu Ala Gly Lys Leu Arg Ser Gly Asp
      35              40              45

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Arg Ser Met Val Glu Val Leu Ala Asp His Pro Gly Glu Leu Val Arg
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				85					90					95		
Val	Pro	Asp	Gly	Thr	Leu	Val	Thr	Val	Met	Ala	Gly	Asn	Asp	Glu	Asn	
			100					105					110			
Tyr	Ser	Ala	Glu	Leu	Arg	Asn	Ala	Thr	Ala	Ala	Met	Lys	Asn	Gln	Val	
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Ala	Arg	Phe	Asn	Asp	Leu	Arg	Phe	Val	Gly	Arg	Ser	Gly	Arg	Gly	Lys	
	130					135					140					
Ser	Phe	Thr	Leu	Thr	Ile	Thr	Val	Phe	Thr	Asn	Pro	Pro	Gln	Val	Ala	
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Thr	Tyr	His	Arg	Ala	Ile	Lys	Ile	Thr	Val	Asp	Gly	Pro	Arg	Glu	Pro	
				165					170					175		
Arg	Asn	Arg	Thr	Glu	Lys	His	Ser	Thr	Met	Pro	Asp	Ser	Pro	Val	Asp	
			180						185					190		
Val	Lys	Thr	Gln	Ser	Arg	Leu	Thr	Pro	Pro	Thr	Met	Pro	Pro	Pro	Pro	
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Thr	Thr	Gln	Gly	Ala	Pro	Arg	Thr	Ser	Ser	Phe	Thr	Pro	Thr	Thr	Leu	
	210					215					220					
Thr	Asn	Gly	Thr	Ser	His	Ser	Pro	Thr	Ala	Leu	Asn	Gly	Ala	Pro	Ser	
225					230					235					240	
Pro	Pro	Asn	Gly	Phe	Ser	Asn	Gly	Pro	Ser	Ser	Ser	Ser	Ser	Ser	Ser	
				245					250					255		
Leu	Ala	Asn	Gln	Gln	Leu	Pro	Pro	Ala	Cys	Gly	Ala	Arg	Gln	Leu	Ser	
		260						265					270			
Lys	Leu	Lys	Arg	Phe	Leu	Thr	Thr	Leu	Gln	Gln	Phe	Gly	Asn	Asp	Ile	
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Ser	Pro	Glu	Ile	Gly	Glu	Arg	Val	Arg	Thr	Leu	Val	Leu	Gly	Leu	Val	
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Asn	Ser	Thr	Leu	Thr	Ile	Glu	Glu	Phe	His	Ser	Lys	Leu	Gln	Glu	Ala	
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Leu	Pro	Leu	Leu	Gln	Arg	Glu	Leu	Leu	His	Cys	Ala	Arg	Leu	Ala	Lys	
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Gln	Asn	Pro	Ala	Gln	Tyr	Leu	Ala	Gln	His	Glu	Gln	Leu	Leu	Leu	Asp	
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370					375					380					
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Phe	Asp	Arg	Glu	Pro	Leu	His	Ser	Glu	His	Pro	Ser	Lys	Arg	Pro	Cys
				405					410					415	
Thr	Ile	Ser	Pro	Gly	Gln	Arg	Tyr	Ser	Pro	Asn	Asn	Gly	Leu	Ser	Tyr
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Arg	Leu	Asp	Asp	Met	Ala	Ile	Ala	His	His	Tyr	Arg	Asp	Ser	Tyr	Arg
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His	Pro	Ser	His	Arg	Asp	Leu	Arg	Asp	Arg	Asn	Arg	Pro	Met	Gly	Leu
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His	Gly	Thr	Arg	Gln	Glu	Glu	Met	Ile	Asp	His	Arg	Leu	Thr	Asp	Arg
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Glu	Trp	Ala	Glu	Glu	Trp	Lys	His	Leu	Asp	His	Leu	Leu	Asn	Cys	Ile
		500						505					510		
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Ser	Arg	Gln	Gln	Ser	Pro	Val	Asn	Pro	Asp	Pro	Val	Ala	Leu	Asp	Ala
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His	Arg	Glu	Phe	Leu	His	Arg	Pro	Ala	Ser	Gly	Tyr	Val	Pro	Glu	Glu
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	610					615					620				
Asp	Met	Ile	Thr	Thr	Glu	Arg	Ala	Lys	Met	Glu	Arg	Thr	Val	Ala	Glu
	625					630					635				640
Ala	Lys	Arg	Gln	Ala	Ala	Glu	Asp	Ala	Leu	Ala	Val	Ile	Asn	Gln	Gln
			645						650					655	
Glu	Asp	Ser	Ser	Glu	Ser	Cys	Trp	Asn	Cys	Gly	Arg	Lys	Ala	Ser	Glu
			660					665					670		
Thr	Cys	Ser	Gly	Cys	Asn	Thr	Ala	Arg	Tyr	Cys	Gly	Ser	Phe	Cys	Gln
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His Lys Asp Trp Glu Lys His His His Ile Cys Gly Gln Thr Leu Gln
 690 695 700

Ala Gln Gln Gln Gly Asp Thr Pro Ala Val Ser Ser Ser Val Thr Pro
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Asn Ser Gly Ala Gly Ser Pro Met Asp Thr Pro Pro Ala Ala Thr Pro
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Arg Ser Thr Thr Pro Gly Thr Pro Ser Thr Ile Glu Thr Thr Pro Arg
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<210> 94

<211> 4272

<212> DNA

<213> Homo sapiens

<400> 94

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<210> 95

<211> 588

<212> PRT

<213> Homo sapiens

<400> 95

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Ser Arg Leu Thr Pro Pro Thr Met Pro Pro Pro Pro Thr Thr Gln Gly
      35                               40                      45

Ala Pro Arg Thr Ser Ser Phe Thr Pro Thr Thr Leu Thr Asn Gly Thr
      50                               55                      60

Ser His Ser Pro Thr Ala Leu Asn Gly Ala Pro Ser Pro Pro Asn Gly
      65                               70                      75                      80

Phe Ser Asn Gly Pro Ser Ser Ser Ser Ser Ser Ser Leu Ala Asn Gln

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85					90					95					
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			100					105					110		
Phe	Leu	Thr	Thr	Leu	Gln	Gln	Phe	Gly	Asn	Asp	Ile	Ser	Pro	Glu	Ile
		115					120					125			
Gly	Glu	Arg	Val	Arg	Thr	Leu	Val	Leu	Gly	Leu	Val	Asn	Ser	Thr	Leu
	130					135					140				
Thr	Ile	Glu	Glu	Phe	His	Ser	Lys	Leu	Gln	Glu	Ala	Thr	Asn	Phe	Pro
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Leu	Arg	Pro	Phe	Val	Ile	Pro	Phe	Leu	Lys	Ala	Asn	Leu	Pro	Leu	Leu
				165					170					175	
Gln	Arg	Glu	Leu	Leu	His	Cys	Ala	Arg	Leu	Ala	Lys	Gln	Asn	Pro	Ala
			180					185					190		
Gln	Tyr	Leu	Ala	Gln	His	Glu	Gln	Leu	Leu	Leu	Asp	Ala	Ser	Thr	Thr
	195						200					205			
Ser	Pro	Val	Asp	Ser	Ser	Glu	Leu	Leu	Leu	Asp	Val	Asn	Glu	Asn	Gly
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Lys	Arg	Arg	Thr	Pro	Asp	Arg	Thr	Lys	Glu	Asn	Gly	Phe	Asp	Arg	Glu
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Pro	Leu	His	Ser	Glu	His	Pro	Ser	Lys	Arg	Pro	Cys	Thr	Ile	Ser	Pro
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Gly	Gln	Arg	Tyr	Ser	Pro	Asn	Asn	Gly	Leu	Ser	Tyr	Gln	Pro	Asn	Gly
			260					265					270		
Leu	Pro	His	Pro	Thr	Pro	Pro	Pro	Pro	Gln	His	Tyr	Arg	Leu	Asp	Asp
		275					280					285			
Met	Ala	Ile	Ala	His	His	Tyr	Arg	Asp	Ser	Tyr	Arg	His	Pro	Ser	His
	290					295					300				
Arg	Asp	Leu	Arg	Asp	Arg	Asn	Arg	Pro	Met	Gly	Leu	His	Gly	Thr	Arg
305					310					315					320
Gln	Glu	Glu	Met	Ile	Asp	His	Arg	Leu	Thr	Asp	Arg	Glu	Trp	Ala	Glu
			325						330					335	
Glu	Trp	Lys	His	Leu	Asp	His	Leu	Leu	Asn	Cys	Ile	Met	Asp	Met	Val
			340					345					350		
Glu	Lys	Thr	Arg	Arg	Ser	Leu	Thr	Val	Leu	Arg	Arg	Cys	Gln	Glu	Ala
		355					360					365			
Asp	Arg	Glu	Glu	Leu	Asn	Tyr	Trp	Ile	Arg	Arg	Tyr	Ser	Asp	Ala	Glu
	370					375					380				
Asp	Leu	Lys	Lys	Gly	Gly	Gly	Ser	Ser	Ser	Ser	His	Ser	Arg	Gln	Gln
385					390					395					400

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Ser Pro Val Asn Pro Asp Pro Val Ala Leu Asp Ala His Arg Glu Phe
405 410 415

Leu His Arg Pro Ala Ser Gly Tyr Val Pro Glu Glu Ile Trp Lys Lys
420 425 430

Ala Glu Glu Ala Val Asn Glu Val Lys Arg Gln Ala Met Thr Glu Leu
435 440 445

Gln Lys Ala Val Ser Glu Ala Glu Arg Lys Ala His Asp Met Ile Thr
450 455 460

Thr Glu Arg Ala Lys Met Glu Arg Thr Val Ala Glu Ala Lys Arg Gln
465 470 475 480

Ala Ala Glu Asp Ala Leu Ala Val Ile Asn Gln Gln Glu Asp Ser Ser
485 490 495

Glu Ser Cys Trp Asn Cys Gly Arg Lys Ala Ser Glu Thr Cys Ser Gly
500 505 510

Cys Asn Thr Ala Arg Tyr Cys Gly Ser Phe Cys Gln His Lys Asp Trp
515 520 525

Glu Lys His His His Ile Cys Gly Gln Thr Leu Gln Ala Gln Gln Gln
530 535 540

Gly Asp Thr Pro Ala Val Ser Ser Ser Val Thr Pro Asn Ser Gly Ala
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Gly Ser Pro Met Asp Thr Pro Pro Ala Ala Thr Pro Arg Ser Thr Thr
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Pro Gly Thr Pro Ser Thr Ile Glu Thr Thr Pro Arg
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<210> 96

<211> 2217

<212> DNA

<213> Homo sapiens

<400> 96

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<210> 97

<211> 231

<212> PRT

<213> Homo sapiens

<400> 97

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Ser Arg Leu Thr Pro Pro Thr Met Pro Pro Pro Pro Thr Thr Gln Gly
                      35                      40                     45

Ala Pro Arg Thr Ser Ser Phe Thr Pro Thr Thr Leu Thr Asn Gly Thr
                      50                      55                     60

Ser His Ser Pro Thr Ala Leu Asn Gly Ala Pro Ser Pro Pro Asn Gly
                      65                      70                     75                     80

Phe Ser Asn Gly Pro Ser Ser Ser Ser Ser Ser Ser Leu Ala Asn Gln
                      85                      90                     95

Gln Leu Pro Pro Ala Cys Gly Ala Arg Gln Leu Ser Lys Leu Lys Arg
                      100                     105                    110

Phe Leu Thr Thr Leu Gln Gln Phe Gly Asn Asp Ile Ser Pro Glu Ile
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Gly Glu Arg Val Arg Thr Leu Val Leu Gly Leu Val Asn Ser Thr Leu
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Gln Arg Glu Leu Leu His Cys Ala Arg Leu Ala Lys Gln Asn Pro Ala
 180 185 190

Gln Tyr Leu Ala Gln His Glu Gln Leu Leu Leu Asp Ala Ser Thr Thr
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Lys Arg Arg Thr Pro Asp Arg
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<210> 98

<211> 1412

<212> DNA

<213> Homo sapiens

<400> 98

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tagatactgt tctatcagat actgtgctct cataactaag aattctaaga aatgtaaaat 1320
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<210> 99

<211> 198

<212> PRT

<213> Homo sapiens

<400> 99

Ser Phe Thr Leu Thr Ile Thr Val Phe Thr Asn Pro Pro Gln Val Ala

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1	5	10	15
Thr Tyr His Arg Ala Ile Lys Ile Thr Val Asp Gly Pro Arg Glu Pro	20	25	30
Arg Asn Arg Thr Glu Lys His Ser Thr Met Pro Asp Ser Pro Val Asp	35	40	45
Val Lys Thr Gln Ser Arg Leu Thr Pro Pro Thr Met Pro Pro Pro Pro	50	55	60
Thr Thr Gln Gly Ala Pro Arg Thr Ser Ser Phe Thr Pro Thr Thr Leu	65	70	75
Thr Asn Gly Thr Ser His Ser Pro Thr Ala Leu Asn Gly Ala Pro Ser	85	90	95
Pro Pro Asn Gly Phe Ser Asn Gly Pro Ser Ser Ser Ser Ser Ser Ser	100	105	110
Leu Ala Asn Gln Gln Leu Pro Pro Ala Cys Gly Ala Arg Gln Leu Ser	115	120	125
Lys Leu Lys Arg Phe Leu Thr Thr Leu Gln Gln Phe Gly Asn Asp Ile	130	135	140
Ser Pro Glu Ile Gly Glu Arg Val Arg Thr Leu Val Leu Gly Leu Val	145	150	155
Asn Ser Thr Leu Thr Ile Glu Glu Phe His Ser Lys Leu Gln Glu Ala	165	170	175
Thr Asn Phe Pro Leu Arg Pro Phe Val Ile Pro Phe Leu Lys Val Leu	180	185	190
His Ser Ser Leu Val Val	195		

<210> 100

<211> 799

<212> DNA

<213> Homo sapiens

<400> 100

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cacaatgccca gactcacctg tggatgtgaa gacgcaatct aggctgactc ctccaacaat 180
gccacctccc ccaactactc aaggagctcc aagaaccagt tcatttacac cgacaacggt 240
aactaatggc acgagccatt ctctacagc cttgaatggc gccccctcac cacccaatgg 300
cttcagcaat gggccttcct cttcttcctc ctctctctg gctaataaac agctgcccc 360
agcctgtggt gccaggcaac tcagcaagct gaaaagggtt cttactaccc tgcagcagtt 420
tggcaatgac atttcacccg agataggaga aagagttcgc accctcgttc tgggactagt 480
gaactccact ttgacaattg aagaatttca ttccaaactg caagaagcta ctaacttccc 540
actgagacct tttgtcatcc catttttgaa ggtattgcac agttcactgg tcgtgtaaag 600
tattttaaac catattgttg ctaggtcata actgtgtgct tttttagtag atttaggggc 660
tctttgattt aatttaatgg atgaaaacta tctgaatcga ttgtatttat gaccatttcc 720
taagtagtct gaaaattaca aggagtgttt taaataatta cctgaaaaga agtaaagttt 780

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84/299

gaagaagagt ttagaagtc

799

<210> 101

<211> 237

<212> DNA

<213> Homo sapiens

<400> 101

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tgtgaagacg caatctaggc tgactcctcc aacaatgcc a cctccccaa ctactcaagg 120
agctccaaga accagttcat ttacaccgac aacgttaact aatggcacga gccattctcc 180
tacagccttg aatggcgccc cctcaccacc caatggcttc agcaatgggc cttcctc 237

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<210> 102

<211> 276

<212> DNA

<213> Homo sapiens

<400> 102

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tcgccacccta ccacagagcc atcaaaatca cagtggatgg gccccgagaa cctcgaaata 120
aaccctactt gaaaaactga ggtgcttaag gagtaaaata atatgttcct ggtggcatcc 180
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<210> 103

<211> 251

<212> PRT

<213> Homo sapiens

<400> 103

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Ser Phe Thr Leu Thr Ile Thr Val Phe Thr Asn Pro Pro Gln Val Ala
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Thr Tyr His Arg Ala Ile Lys Ile Thr Val Asp Gly Pro Arg Glu Pro
      20              25              30

Arg Asn Arg Thr Glu Lys His Ser Thr Met Pro Asp Ser Pro Val Asp
      35              40              45

Val Lys Thr Gln Ser Arg Leu Thr Pro Pro Thr Met Pro Pro Pro Pro
 50              55              60

Thr Thr Gln Gly Ala Pro Arg Thr Ser Ser Phe Thr Pro Thr Thr Leu
 65              70              75              80

Thr Asn Gly Thr Ser His Ser Pro Thr Ala Leu Asn Gly Ala Pro Ser
      85              90              95

Pro Pro Asn Gly Phe Ser Asn Gly Pro Ser Ser Ser Ser Ser Ser Ser
      100              105              110

Leu Ala Asn Gln Gln Leu Pro Pro Ala Cys Gly Ala Arg Gln Leu Ser
      115              120              125

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Lys Leu Lys Arg Phe Leu Thr Thr Leu Gln Gln Phe Gly Asn Asp Ile
 130 135 140
 Ser Pro Glu Ile Gly Glu Arg Val Arg Thr Leu Val Leu Gly Leu Val
 145 150 155 160
 Asn Ser Thr Leu Thr Ile Glu Glu Phe His Ser Lys Leu Gln Glu Ala
 165 170 175
 Thr Asn Phe Pro Leu Arg Pro Phe Val Ile Pro Phe Leu Lys Ala Asn
 180 185 190
 Leu Pro Leu Leu Gln Arg Glu Leu Leu His Cys Ala Arg Leu Ala Lys
 195 200 205
 Gln Asn Pro Ala Gln Tyr Leu Ala Gln His Glu Gln Leu Leu Leu Asp
 210 215 220
 Ala Ser Thr Thr Ser Pro Val Asp Ser Ser Glu Leu Leu Leu Asp Val
 225 230 235 240
 Asn Glu Asn Gly Lys Arg Arg Thr Pro Asp Arg
 245 250

<210> 104

<211> 1446

<212> DNA

<213> Homo sapiens

<400> 104

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cacaatgccca gactcacctg tggatgtgaa gacgcaatct aggctgactc ctccaacaat 180
gccacctccc ccaactactc aaggagctcc aagaaccagt tcatttacac cgacaacggt 240
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actgagacct tttgtcatcc catttttgaa ggccaacttg cccctgctgc agcgtgagct 600
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<210> 105

<211> 1395

<212> PRT

<213> Homo sapiens

<400> 105

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      20              25              30

Ala Pro Asp Ala Gly Ala Ala Leu Ala Gly Lys Leu Arg Ser Gly Asp
      35              40              45

Arg Ser Met Val Glu Val Leu Ala Asp His Pro Gly Glu Leu Val Arg
      50              55              60

Thr Asp Ser Pro Asn Phe Leu Cys Ser Val Leu Pro Thr His Trp Arg
      65              70              75              80

Cys Asn Lys Thr Leu Pro Ile Ala Phe Lys Val Val Ala Leu Gly Asp
      85              90              95

Val Pro Asp Gly Thr Leu Val Thr Val Met Ala Gly Asn Asp Glu Asn
      100              105              110

Tyr Ser Ala Glu Leu Arg Asn Ala Thr Ala Ala Met Lys Asn Gln Val
      115              120              125

Ala Arg Phe Asn Asp Leu Arg Phe Val Gly Arg Ser Gly Arg Gly Lys
      130              135              140

Ser Phe Thr Leu Thr Ile Thr Val Phe Thr Asn Pro Pro Gln Val Ala
      145              150              155              160

Thr Tyr His Arg Ala Ile Lys Ile Thr Val Asp Gly Pro Arg Glu Pro
      165              170              175

Arg Asn Asn Glu Cys Val Tyr Gly Asn Tyr Pro Glu Ile Pro Leu Glu
      180              185              190

Glu Met Pro Asp Ala Asp Gly Val Ala Ser Thr Pro Ser Leu Asn Ile
      195              200              205

Gln Glu Pro Cys Ser Pro Ala Thr Ser Ser Glu Ala Phe Thr Pro Lys
      210              215              220

Glu Gly Ser Pro Tyr Lys Ala Pro Ile Tyr Ile Pro Asp Asp Ile Pro
      225              230              235              240

Ile Pro Ala Glu Phe Glu Leu Arg Glu Ser Asn Met Pro Gly Ala Gly
      245              250              255

Leu Gly Ile Trp Thr Lys Arg Lys Ile Glu Val Gly Glu Lys Phe Gly
      260              265              270

Pro Tyr Val Gly Glu Gln Arg Ser Asn Leu Lys Asp Pro Ser Tyr Gly

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275					280					285					
Trp	Glu	Ile	Leu	Asp	Glu	Phe	Tyr	Asn	Val	Lys	Phe	Cys	Ile	Asp	Ala
290						295					300				
Ser	Gln	Pro	Asp	Val	Gly	Ser	Trp	Leu	Lys	Tyr	Ile	Arg	Phe	Ala	Gly
305					310					315					320
Cys	Tyr	Asp	Gln	His	Asn	Leu	Val	Ala	Cys	Gln	Ile	Asn	Asp	Gln	Ile
				325					330					335	
Phe	Tyr	Arg	Val	Val	Ala	Asp	Ile	Ala	Pro	Gly	Glu	Glu	Leu	Leu	Leu
			340					345					350		
Phe	Met	Lys	Ser	Glu	Asp	Tyr	Pro	His	Glu	Thr	Met	Ala	Pro	Asp	Ile
		355					360					365			
His	Glu	Glu	Arg	Gln	Tyr	Arg	Cys	Glu	Asp	Cys	Asp	Gln	Leu	Phe	Glu
	370					375					380				
Ser	Lys	Ala	Glu	Leu	Ala	Asp	His	Gln	Lys	Phe	Pro	Cys	Ser	Thr	Pro
385					390					395					400
His	Ser	Ala	Phe	Ser	Met	Val	Glu	Glu	Asp	Phe	Gln	Gln	Lys	Leu	Glu
				405					410					415	
Ser	Glu	Asn	Asp	Leu	Gln	Glu	Ile	His	Thr	Ile	Gln	Glu	Cys	Lys	Glu
			420					425					430		
Cys	Asp	Gln	Val	Phe	Pro	Asp	Leu	Gln	Ser	Leu	Glu	Lys	His	Met	Leu
	435						440					445			
Ser	His	Thr	Glu	Glu	Arg	Glu	Tyr	Lys	Cys	Asp	Gln	Cys	Pro	Lys	Ala
	450					455					460				
Phe	Asn	Trp	Lys	Ser	Asn	Leu	Ile	Arg	His	Gln	Met	Ser	His	Asp	Ser
465					470					475					480
Gly	Lys	His	Tyr	Glu	Cys	Glu	Asn	Cys	Ala	Lys	Val	Phe	Thr	Asp	Pro
				485					490					495	
Ser	Asn	Leu	Gln	Arg	His	Ile	Arg	Ser	Gln	His	Val	Gly	Ala	Arg	Ala
			500					505					510		
His	Ala	Cys	Pro	Glu	Cys	Gly	Lys	Thr	Phe	Ala	Thr	Ser	Ser	Gly	Leu
	515						520					525			
Lys	Gln	His	Lys	His	Ile	His	Ser	Ser	Val	Lys	Pro	Phe	Ile	Cys	Glu
	530					535					540				
Val	Cys	His	Lys	Ser	Tyr	Thr	Gln	Phe	Ser	Asn	Leu	Cys	Arg	His	Lys
545					550					555					560
Arg	Met	His	Ala	Asp	Cys	Arg	Thr	Gln	Ile	Lys	Cys	Lys	Asp	Cys	Gly
				565					570					575	
Gln	Met	Phe	Ser	Thr	Thr	Ser	Ser	Leu	Asn	Lys	His	Arg	Arg	Phe	Cys
			580					585					590		

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Glu Gly Lys Asn His Phe Ala Ala Gly Gly Phe Phe Gly Gln Gly Ile
 595 600 605
 Ser Leu Pro Gly Thr Pro Ala Met Asp Lys Thr Ser Met Val Asn Met
 610 615 620
 Ser His Ala Asn Pro Gly Leu Ala Asp Tyr Phe Gly Ala Asn Arg His
 625 630 635 640
 Pro Ala Gly Leu Thr Phe Pro Thr Ala Pro Gly Phe Ser Phe Ser Phe
 645 650 655
 Pro Gly Leu Phe Pro Ser Gly Leu Tyr His Arg Pro Pro Leu Ile Pro
 660 665 670
 Ala Ser Ser Pro Val Lys Gly Leu Ser Ser Thr Glu Gln Thr Asn Lys
 675 680 685
 Ser Gln Ser Pro Leu Met Thr His Pro Gln Ile Leu Pro Ala Thr Gln
 690 695 700
 Asp Ile Leu Lys Ala Leu Ser Lys His Pro Ser Val Gly Asp Asn Lys
 705 710 715 720
 Pro Val Glu Leu Gln Pro Glu Arg Ser Ser Glu Glu Arg Pro Phe Glu
 725 730 735
 Lys Ile Ser Asp Gln Ser Glu Ser Ser Asp Leu Asp Asp Val Ser Thr
 740 745 750
 Pro Ser Gly Ser Asp Leu Glu Thr Thr Ser Gly Ser Asp Leu Glu Ser
 755 760 765
 Asp Ile Glu Ser Asp Lys Glu Lys Phe Lys Glu Asn Gly Lys Met Phe
 770 775 780
 Lys Asp Lys Val Ser Pro Leu Gln Asn Leu Ala Ser Ile Asn Asn Lys
 785 790 795 800
 Lys Glu Tyr Ser Asn His Ser Ile Phe Ser Pro Ser Leu Glu Glu Gln
 805 810 815
 Thr Ala Val Ser Gly Ala Val Asn Asp Ser Ile Lys Ala Ile Ala Ser
 820 825 830
 Ile Ala Glu Lys Tyr Phe Gly Ser Thr Gly Leu Val Gly Leu Gln Asp
 835 840 845
 Lys Lys Val Gly Ala Leu Pro Tyr Pro Ser Met Phe Pro Leu Pro Phe
 850 855 860
 Phe Pro Ala Phe Ser Gln Ser Met Tyr Pro Phe Pro Asp Arg Asp Leu
 865 870 875 880
 Arg Ser Leu Pro Leu Lys Met Glu Pro Gln Ser Pro Gly Glu Val Lys
 885 890 895

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Lys Leu Gln Lys Gly Ser Ser Glu Ser Pro Phe Asp Leu Thr Thr Lys
 900 905 910
 Arg Lys Asp Glu Lys Pro Leu Thr Pro Val Pro Ser Lys Pro Pro Val
 915 920 925
 Thr Pro Ala Thr Ser Gln Asp Gln Pro Leu Asp Leu Ser Met Gly Ser
 930 935 940
 Arg Ser Arg Ala Ser Gly Thr Lys Leu Thr Glu Pro Arg Lys Asn His
 945 950 955 960
 Val Phe Gly Gly Lys Lys Gly Ser Asn Val Glu Ser Arg Pro Ala Ser
 965 970 975
 Asp Gly Ser Leu Gln His Ala Arg Pro Thr Pro Phe Phe Met Asp Pro
 980 985 990
 Ile Tyr Arg Val Glu Lys Arg Lys Leu Thr Asp Pro Leu Glu Ala Leu
 995 1000 1005
 Lys Glu Lys Tyr Leu Arg Pro Ser Pro Gly Phe Leu Phe His Pro Gln
 1010 1015 1020
 Met Ser Ala Ile Glu Asn Met Ala Glu Lys Leu Glu Ser Phe Ser Ala
 1025 1030 1035 1040
 Leu Lys Pro Glu Ala Ser Glu Leu Leu Gln Ser Val Pro Ser Met Phe
 1045 1050 1055
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 1060 1065 1070
 Gly Lys Glu Arg Tyr Thr Cys Arg Tyr Cys Gly Lys Ile Phe Pro Arg
 1075 1080 1085
 Ser Ala Asn Leu Thr Arg His Leu Arg Thr His Thr Gly Glu Gln Pro
 1090 1095 1100
 Tyr Arg Cys Lys Tyr Cys Asp Arg Ser Phe Ser Ile Ser Ser Asn Leu
 1105 1110 1115 1120
 Gln Arg His Val Arg Asn Ile His Asn Lys Glu Lys Pro Phe Lys Cys
 1125 1130 1135
 His Leu Cys Asp Arg Cys Phe Gly Gln Gln Thr Asn Leu Asp Arg His
 1140 1145 1150
 Leu Lys Lys His Glu Asn Gly Asn Met Ser Gly Thr Ala Thr Ser Ser
 1155 1160 1165
 Pro His Ser Glu Leu Glu Ser Thr Gly Ala Ile Leu Asp Asp Lys Glu
 1170 1175 1180
 Asp Ala Tyr Phe Thr Glu Ile Arg Asn Phe Ile Gly Asn Ser Asn His
 1185 1190 1195 1200
 Gly Ser Gln Ser Pro Arg Asn Val Glu Glu Arg Met Asn Gly Ser His

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1205	1210	1215
Phe Lys Asp Glu Lys Ala Leu Val Thr Ser Gln Asn Ser Asp Leu Leu 1220	1225	1230
Asp Asp Glu Glu Val Glu Asp Glu Val Leu Leu Asp Glu Glu Asp Glu 1235	1240	1245
Asp Asn Asp Ile Thr Gly Lys Thr Gly Lys Glu Pro Val Thr Ser Asn 1250	1255	1260
Leu His Glu Gly Asn Pro Glu Asp Asp Tyr Glu Glu Thr Ser Ala Leu 1265	1270	1275
Glu Met Ser Cys Lys Thr Ser Pro Val Arg Tyr Lys Glu Glu Glu Tyr 1285	1290	1295
Lys Ser Gly Leu Ser Ala Leu Asp His Ile Arg His Phe Thr Asp Ser 1300	1305	1310
Leu Lys Met Arg Lys Met Glu Asp Asn Gln Tyr Ser Glu Ala Glu Leu 1315	1320	1325
Ser Ser Phe Ser Thr Ser His Val Pro Glu Glu Leu Lys Gln Pro Leu 1330	1335	1340
His Arg Lys Ser Lys Ser Gln Ala Tyr Ala Met Met Leu Ser Leu Ser 1345	1350	1355
Asp Lys Glu Ser Leu His Ser Thr Ser His Ser Ser Ser Asn Val Trp 1365	1370	1375
His Ser Met Ala Arg Ala Ala Ala Glu Ser Ser Ala Ile Gln Ser Ile 1380	1385	1390
Ser His Val 1395		

<210> 106

<211> 5938

<212> DNA

<213> Homo sapiens

<400> 106

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<210> 107

<211> 261

<212> PRT

<213> Homo sapiens

<400> 107

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Thr Pro Pro Ser Thr Ala Leu Ser Pro Gly Lys Met Ser Glu Ala Leu
      20                      25                      30

Pro Leu Gly Ala Pro Asp Ala Gly Ala Ala Leu Ala Gly Lys Leu Arg
      35                      40                      45

Ser Gly Asp Arg Ser Met Val Glu Val Leu Ala Asp His Pro Gly Glu
      50                      55                      60

Leu Val Arg Thr Asp Ser Pro Asn Phe Leu Cys Ser Val Leu Pro Thr
      65                      70                      75                      80

His Trp Arg Cys Asn Lys Thr Leu Pro Ile Ala Phe Lys Val Val Ala
      85                      90                      95

Leu Gly Asp Val Pro Asp Gly Thr Leu Val Thr Val Met Ala Gly Asn
      100                      105                      110

Asp Glu Asn Tyr Ser Ala Glu Leu Arg Asn Ala Thr Ala Ala Met Lys

```

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115	120	125
Asn Gln Val Ala Arg Phe	Asn Asp Leu Arg Phe	Val Gly Arg Ser Gly
130	135	140
Arg Gly Lys Ser Phe Thr	Leu Thr Ile Thr Val	Phe Thr Asn Pro Pro
145	150	155
Gln Val Ala Thr Tyr His	Arg Ala Ile Lys Ile	Thr Val Asp Gly Pro
165	170	175
Arg Glu Pro Arg Arg His	Arg Gln Lys Leu Asp	Asp Gln Thr Lys Pro
180	185	190
Gly Ser Leu Ser Phe Ser	Glu Arg Leu Ser Glu	Leu Glu Gln Leu Arg
195	200	205
Arg Thr Ala Met Arg Val	Ser Pro His His Pro	Ala Pro Thr Pro Asn
210	215	220
Pro Arg Ala Ser Leu Asn	His Ser Thr Ala Phe	Asn Pro Gln Pro Gln
225	230	235
Ser Gln Met Gln Glu Ser	Trp Met Leu Pro Ile	Leu Ser Ser Phe Cys
245	250	255
Lys Lys Gly Ser Lys		
260		

<210> 108

<211> 1025

<212> DNA

<213> Homo sapiens

<400> 108

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gctgccctgg ccggcaagct gaggagcggc gaccgcagca tgggtggaggt gctggccgac 180
caccggggag agctgggtgc caccgacagc cccaacttcc tctgctccgt gctgcctacg 240
cactggcgct gcaacaagac cctgcccatc gctttcaagg tgggtggccct aggggatgtt 300
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caagtgcgca cctaccacag agccatcaaa atcacagtgg atgggccccg agaacctcga 540
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cccacgcca accctcgtgc ctccctgaac cactccactg cctttaacct tcagcctcag 720
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gcaagatcac cgtgacatcc gaggtgcctt tctccaaaag gtatttgaaa tatctacca 900
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agagttacga attacgttac ttccagatta accaggacga agaagaggag gaagacgagg 1020
attaa                                           1025

```

<210> 109

<211> 470

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<212> DNA

<213> Homo sapiens

<400> 109

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accgcaagtc gccacctacc acagagccat caaaatcaca gtggatgggc cccgagaacc 120
tcgaaaatca tggatgctgc caattttgag cagtttttgc aagaaaggat caaagtgaac 180
ggaaaagctg ggaaccttgg tggaggggtg gtgaccatcg aaaggagcaa gagcaagatc 240
accgtgacat ccgaggtgcc tttctccaaa aggtatttga aatatctcac caaaaaatat 300
ttgaagaaga ataatctacg tgactgggtg cgcgtagttg ctaacagcaa agagagttac 360
gaattacgtt acttccagat taaccaggac gaagaagagg aggaagacga ggattaaatt 420
tcatttatct ggaaaatttt gtatgagttc ttgaataaaa cttgggaacc 470
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<210> 110

<211> 17

<212> PRT

<213> Homo sapiens

<400> 110

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Gly Met Gly Gly Ser Asp Arg Gly Gly Phe Asn Lys Phe Gly Gly Ser
  1                      5                      10                      15
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Gly

<210> 111

<211> 55

<212> DNA

<213> Homo sapiens

<400> 111

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<210> 112

<211> 32

<212> PRT

<213> Homo sapiens

<400> 112

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Gly Met Gly Arg Trp Lys Leu His Val Leu Ser Ser Asn Leu Ser Ser
  1                      5                      10                      15
```

```
Pro Ala Glu Val Thr Val Val Ala Ser Ile Asn Leu Val Ala Val Ala
      20                      25                      30
```

<210> 113

<211> 99

<212> DNA

<213> Homo sapiens

<400> 113

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tgaccgtggg ggcttcaata aatttgggtg cagtggcca 99
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<210> 114
<211> 120
<212> DNA
<213> Homo sapiens
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<210> 115 .
<211> 375
<212> PRT
<213> Homo sapiens
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<400> 115															
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Pro	Ala	Ser	Glu	Lys	Glu	Pro	Glu	Met	Pro	Gly	Pro	Arg	Glu	Glu	Ser
			20					25					30		
Glu	Glu	Glu	Glu	Asp	Glu	Asp	Asp	Glu	Glu	Glu	Glu	Glu	Glu	Glu	Lys
		35					40					45			
Glu	Lys	Ser	Leu	Ile	Val	Glu	Gly	Lys	Arg	Glu	Lys	Lys	Lys	Val	Glu
	50					55					60				
Arg	Leu	Thr	Met	Gln	Val	Ser	Ser	Leu	Gln	Arg	Glu	Pro	Phe	Thr	Ile
65					70					75					80
Ala	Gln	Gly	Lys	Gly	Gln	Lys	Leu	Cys	Glu	Ile	Glu	Arg	Ile	His	Phe
				85					90					95	
Phe	Leu	Ser	Lys	Lys	Lys	Thr	Asp	Glu	Leu	Arg	Asn	Leu	His	Lys	Leu
			100					105					110		
Leu	Tyr	Asn	Arg	Pro	Gly	Thr	Val	Ser	Ser	Leu	Lys	Lys	Asn	Val	Gly
		115					120					125			
Gln	Phe	Ser	Gly	Phe	Pro	Phe	Glu	Lys	Gly	Ser	Val	Gln	Tyr	Lys	Lys
	130					135					140				
Lys	Glu	Glu	Met	Leu	Lys	Lys	Phe	Arg	Asn	Ala	Met	Leu	Lys	Ser	Ile
145				150						155					160
Cys	Glu	Val	Leu	Asp	Leu	Glu	Arg	Ser	Gly	Val	Asn	Ser	Glu	Leu	Val
				165					170					175	
Lys	Arg	Ile	Leu	Asn	Phe	Leu	Met	His	Pro	Lys	Pro	Ser	Gly	Lys	Pro
			180					185					190		
Leu	Pro	Lys	Ser	Lys	Lys	Thr	Cys	Ser	Lys	Gly	Ser	Lys	Lys	Glu	Arg
		195					200					205			
Asn	Ser	Ser	Gly	Met	Ala	Arg	Lys	Ala	Lys	Arg	Thr	Lys	Cys	Pro	Glu
	210					215					220				

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Ile Leu Ser Asp Glu Ser Ser Ser Asp Glu Asp Glu Lys Lys Asn Lys
 225 230 235 240

Glu Glu Ser Ser Asp Asp Glu Asp Lys Glu Ser Glu Glu Glu Pro Pro
 245 250 255

Lys Lys Thr Ala Lys Arg Glu Lys Pro Lys Gln Lys Ala Thr Ser Lys
 260 265 270

Ser Lys Lys Ser Val Lys Ser Ala Asn Val Lys Lys Ala Asp Ser Ser
 275 280 285

Thr Thr Lys Lys Asn Gln Asn Ser Ser Lys Lys Glu Ser Glu Ser Glu
 290 295 300

Asp Ser Ser Asp Asp Glu Pro Leu Ile Lys Lys Leu Lys Lys Pro Pro
 305 310 315 320

Thr Asp Glu Glu Leu Lys Glu Thr Ile Lys Lys Leu Leu Ala Ser Ala
 325 330 335

Asn Leu Glu Glu Val Thr Met Lys Gln Ile Cys Lys Lys Val Tyr Glu
 340 345 350

Asn Tyr Pro Thr Tyr Asp Leu Thr Glu Arg Lys Asp Phe Ile Lys Thr
 355 360 365

Thr Val Lys Glu Leu Ile Ser
 370 375

<210> 116

<211> 2699

<212> DNA

<213> Homo sapiens

<220>

<221> modified_base

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<223> a, c, t, g, other or unknown

<400> 116

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gaggagagcg aggaggaaga ggacgaggac gacgaggagg aggaggagga ggaaaaagaa 180
aagagtctca tcgtggaagg caagagggaa aagaaaaaag tagagagggt gacaatgcaa 240
gtctcttcct tacagagaga gccatttaca attgcacaag gaaaggggca gaaactttgt 300
gaaattgaga ggatacattt ttttctaagt aagaagaaaa ccatgaact tagaaatcta 360
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```

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gtctatgaaa attatcctac ttatgattta actgaaagaa aagatttcat aaaaacaact 1140
gtaaaagagc taatttcctg agatagagga cagagaagat gactcgttcc catagatttg 1200
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<210> 117

<211> 288

<212> DNA

<213> Homo sapiens

<400> 117

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acaaatgagc atttctcaa tgggaagacg tcttatatgt tctatgctgt gaatagatag 180
gtttagaatt actttcagca ccgttttgct tccattacag ttaattttat ggggtgggaga 240
gcaaaatcta aatggatgca ctgtctgagt accagaatga atggaaaa 288

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<210> 118

<211> 277

<212> PRT

<213> Homo sapiens

<400> 118

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His Asp Gly Ala Asp Glu Thr Ser Glu Lys Glu Gln Gln Glu Ala Ile
      20                      25                      30

Glu His Ile Asp Glu Val Gln Asn Glu Ile Asp Arg Leu Asn Glu Gln
      35                      40                      45

```

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Ala Ser Glu Glu Ile Leu Lys Val Glu Gln Lys Tyr Asn Lys Leu Arg
 50 55 60
 Gln Pro Phe Phe Gln Lys Arg Ser Glu Leu Ile Ala Lys Ile Pro Asn
 65 70 75 80
 Phe Trp Val Thr Thr Phe Val Asn His Pro Gln Val Ser Ala Leu Leu
 85 90 95
 Gly Glu Glu Asp Glu Glu Ala Leu His Tyr Leu Thr Arg Val Glu Val
 100 105 110
 Thr Glu Phe Glu Asp Ile Lys Ser Gly Tyr Arg Ile Asp Phe Tyr Phe
 115 120 125
 Asp Glu Asn Pro Tyr Phe Glu Asn Lys Val Leu Ser Lys Glu Phe His
 130 135 140
 Leu Asn Glu Ser Gly Asp Pro Ser Ser Lys Ser Thr Glu Ile Lys Trp
 145 150 155 160
 Lys Ser Gly Lys Asp Leu Thr Lys Arg Ser Ser Gln Thr Gln Asn Lys
 165 170 175
 Ala Ser Arg Lys Arg Gln His Glu Glu Pro Glu Ser Phe Phe Thr Trp
 180 185 190
 Phe Thr Asp His Ser Asp Ala Gly Ala Asp Glu Leu Gly Glu Val Ile
 195 200 205
 Lys Asp Asp Ile Trp Pro Asn Pro Leu Gln Tyr Tyr Leu Val Pro Asp
 210 215 220
 Met Asp Asp Glu Glu Gly Glu Gly Glu Glu Asp Asp Asp Asp Asp Glu
 225 230 235 240
 Glu Glu Glu Gly Leu Glu Asp Ile Asp Glu Glu Gly Asp Glu Asp Glu
 245 250 255
 Gly Glu Glu Asp Glu Asp Asp Asp Glu Gly Glu Glu Gly Glu Glu Asp
 260 265 270
 Glu Gly Glu Asp Asp
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<210> 119

<211> 2577

<212> DNA

<213> Homo sapiens

<400> 119

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 aatgaaatag acagacttaa tgaacaagcc agtgaggaga ttttgaaagt agaacagaaa 180
 tataacaaac tccgccaacc attttttcag aagagggtcag aattgatcgc caaaatccca 240
 aattttttggg taacaacatt tgtcaaccat ccacaagtgt ctgcactgct tggggaggaa 300

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ttgtgccctt gattttttat tccaagtggc agttttttaa attggccttt tacctggata 2040
taaattaatt gtgcctgcca ccaccatcca acagacctgg tgctctaatt ccaagtata 2100
cacgggacag ttgctggcat gtcttcattg gctctctaaa atgtggccaa gaagataggc 2160
tctcagtaag aagtctgatg gtgagcagta actgtccctg ctttctggta taaagctctc 2220
aaatgtgacc atgtgaatct ggggtgggata atggactcag ctctgtctgc tcaatgccat 2280
tgtgcagaga agcaccctaa tgcataagct ttttaatgct gtaaaatata gtcgctgaaa 2340
ttaaatgcca ctttttcaga ggtgaattaa tggacagtct ggtgaacttc aaaagctttt 2400
tgatgtataa aacttgataa atggaactat tccatcaata ggcaaaagtg taacaacctc 2460
tctagatgga tagtatgtaa tttctgcaca ggtctctgtt tagtaaatac atcactgtat 2520
accgatcagg aatcttgctc caataaagga acataaagat ttaaaaaaaaa aaaaaaa 2577

```

<210> 120

<211> 288

<212> PRT

<213> Homo sapiens

<400> 120

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Ala Leu Ser Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser
  1              5              10              15

Thr Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln
  20              25              30

Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg
  35              40              45

Met Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys
  50              55              60

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His Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu
 65 70 75 80
 Asn Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile
 85 90 95
 Ser Asn Ile Asn Val Ile Val Leu Glu Leu Lys Met Ala Gly Gln Cys
 100 105 110
 Ser Gln Asn Glu Tyr Phe Asp Ser Leu Leu His Ala Cys Ile Pro Cys
 115 120 125
 Gln Leu Arg Cys Ser Ser Asn Thr Pro Pro Leu Thr Cys Gln Arg Tyr
 130 135 140
 Cys Asn Ala Ser Val Thr Asn Ser Val Lys Gly Thr Asn Ala Ile Leu
 145 150 155 160
 Trp Thr Cys Leu Gly Leu Ser Leu Ile Ile Ser Leu Ala Val Phe Val
 165 170 175
 Leu Met Phe Leu Leu Arg Lys Ile Ser Ser Glu Pro Leu Lys Asp Glu
 180 185 190
 Phe Lys Asn Thr Gly Ser Gly Leu Leu Gly Met Ala Asn Ile Asp Leu
 195 200 205
 Glu Lys Ser Arg Thr Gly Asp Glu Ile Ile Leu Pro Arg Gly Leu Glu
 210 215 220
 Tyr Thr Val Glu Glu Cys Thr Cys Glu Asp Cys Ile Lys Ser Lys Pro
 225 230 235 240
 Lys Val Asp Ser Asp His Cys Phe Pro Leu Pro Ala Met Glu Glu Gly
 245 250 255
 Ala Thr Ile Leu Val Thr Thr Lys Thr Asn Asp Tyr Cys Lys Ser Leu
 260 265 270
 Pro Ala Ala Leu Ser Ala Thr Glu Ile Glu Lys Ser Ile Ser Ala Arg
 275 280 285

<210> 121

<211> 1073

<212> DNA

<213> Homo sapiens

<400> 121

gcactaagtc ttgcacttgt cacaaacagt gcacctactt caagttctac aaagaaaaca 60
 cagctacaac tggagcathtt actgctggat ttacagatga ttttgaatgg aattaataat 120
 tacaagaatc ccaaactcac caggatgctc acatttaagt tttacatgcc caagaaggcc 180
 acagaactga aacatcttca gtgtctagaa gaagaactca aacctctgga ggaagtgcta 240
 aatttagctc aaagcaaaaa ctttacttta agaccaggagg acttaatcag caatatcaac 300
 gtaatagttc tgggaactaaa gatggctggg cagtgcctccc aaaatgaata ttttgacagt 360
 ttgttgcatg cttgcataacc ttgtcaactt cgatgttctt ctaatactcc tcctctaaca 420
 tgtcagcgtt attgtaatgc aagtgtgacc aattcagtga aaggaacgaa tgcgattctc 480
 tggacctgtt tgggactgag cttaataatt tctttggcag ttttcgtgct aatgtttttg 540

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```

ctaaggaaga taagctctga accattaaag gacgagttta aaaacacagg atcaggtctc 600
ctgggcatgg ctaacattga cctggaaaag agcaggactg gtgatgaaat tattcttccg 660
agaggcctcg agtacacggg ggaagaatgc acctgtgaag actgcatcaa gagcaaaccg 720
aaggctcgact ctgaccattg ctttccactc ccagctatgg aggaaggcgc aaccattctt 780
gtcaccacga aaacgaatga ctattgcaag agcctgccag ctgctttgag tgcacggag 840
atagagaaat caatttctgc taggtaatta accatttcga ctcgagcagt gccacttta 900
aaatcttttg tcagaataga tgatgtgtca gatctcttta ggatgactgt atttttcagt 960
tgccgatata gctttttgtc ctctaactgt ggaaactctt tatgttagat atatttctct 1020
aggttactgt tgggagctta atggtagaaa cttccttggt ttctatgatt aaa 1073

```

<210> 122

<211> 26

<212> PRT

<213> Homo sapiens

<400> 122

```

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Phe Lys
  1                      5                      10                      15

```

```

Arg Ala Lys Ala Asn Leu Asp Lys Asn Lys
          20                      25

```

<210> 123

<211> 78

<212> DNA

<213> Homo sapiens

<400> 123

```

gaatttgaag atagagacag gtctcatcgg gaggaatgg agttcaagag ggccaaggcg 60
aacctagaca agaataag                                     78

```

<210> 124

<211> 34

<212> PRT

<213> Homo sapiens

<400> 124

```

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Val His
  1                      5                      10                      15

```

```

Glu Leu Glu Lys Ser Lys Arg Ala Leu Glu Thr Gln Met Glu Glu Met
          20                      25                      30

```

Lys Thr

<210> 125

<211> 102

<212> DNA

<213> Homo sapiens

<400> 125

```

gaatttgaag atagagacag gtctcatcgg gaggaatgg aggtccatga gctggagaag 60
tccaagcggg ccctggagac ccagatggag gagatgaaga cg 102

```

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<210> 126

<211> 50

<212> PRT

<213> Homo sapiens

<400> 126

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Asn Glu
1 5 10 15

Val Glu Ser Val Thr Gly Met Leu Asn Glu Ala Glu Gly Lys Ala Ile
20 25 30

Lys Leu Ala Lys Asp Val Ala Ser Leu Ser Ser Gln Leu Gln Asp Thr
35 40 45

Gln Glu
50

<210> 127

<211> 152

<212> DNA

<213> Homo sapiens

<400> 127

gaattttgaag atagagacag gtctcatcgg gaggaatgg agaatgaagt tgagagcgctc 60
acaggggatgc ttaacgaggc cgaggggaag gccattaagc tggccaagga cgtggcgctcc 120
ctcagttccc agctccagga caccaggag tt 152

<210> 128

<211> 1353

<212> DNA

<213> Homo sapiens

<220>

<221> modified_base

<222> (941)

<223> a, c, t, g, other or unknown

<220>

<221> modified_base

<222> (1067)

<223> a, c, t, g, other or unknown

<220>

<221> modified_base

<222> (1077)

<223> a, c, t, g, other or unknown

<400> 128

cttggccaac attctggagg cagtaaagaa agcttataga ataaccacat attagaactt 60
gtgaaggaga aaatatacat atatataat gtatatatat agtctctcta ttaagtaatt 120
taccataagg ggtttaaata ggaatgtttt ctccaaagtg aatcttgaaa tcttgggtgtt 180
tataattgtc aagcctcttt ttttaaaata gatttgggtca acaggaagta tttttttcta 240
attttttatt tatagaccta gtcaagcttc ttaattgtta aatattgtta taacaataca 300
tctggggcgg gcgcggtggc tcactcctgt aatcccagca ctttgggagg ccagggcggg 360

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```

tgaatcacga ggtcaggaga ttgagaccat cctggctaac acaaagaaac cccatctcta 420
ctaaaaatac aaaaaaattag ctgggagagg aggagggcgc ctgtagtccc agctactcgg 480
gaggcggagc ttgcggtgag ccaagatcgc gccactgcac tccagcgact ccgtctcaaa 540
aaaaaaaaaa aaaaaaacatc tgagtcggtta catggttggt agccgaggag aaaaacatct 600
cttccaaata cgcggtatgag agggacagag ctgaggcaga agccagggag aaggaaacca 660
aggccctgtc cctggctcgg gcccttgaag aggccttgga agccaaagag gaactcgagc 720
ggaccaacaa aatgctcaaa gccgaaatgg aagacctggg cagctccaag gatgacgtgg 780
gcaagaacgt aagtggctct ggggtggtttt tctcgtccat gtttcgcctg cccaccctct 840
gtgctattca ccagtcocatg cgaggctagc tcctggcctt tttcatagcg aactatcatc 900
ggaaatggaa ggaggttttt ggactgggtgc aggggctaaa naggggctga gaatggcagt 960
cgaggatggg tctgagtttg ggggtccgag gataaggctg ggggtctgaac tctcaggggt 1020
catcttgagt cccggccatg catcctgttg gaggccaaag ccacctnccc tgatctnctt 1080
gaggtgccgc tcacgggtggg tttctcaatc gtcttcatga agttgagcct catagaatgg 1140
ggctgcccgc tctgccggca ggtccatgag ctggagaagt ccaagcgggc cctggagacc 1200
cagatggagg agatgaagac gcagctggaa gagctggagg acgagctgca agccacggag 1260
gacgccaaac tgcggctgga agtcaacatg caggcgctca agggccagtt cgaaagggat 1320
ctccaagccc gggacgagca gaatgaggag aag                                     1353

```

<210> 129

<211> 744

<212> DNA

<213> Homo sapiens

<220>

<221> modified_base

<222> (326)

<223> a, c, t, g, other or unknown

<220>

<221> modified_base

<222> (614)

<223> a, c, t, g, other or unknown

<400> 129

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gccgggctta aaatttagta tcttttagtg attgctagat ctctttgtca gtgagttaat 60
taatctaata ggctgatagc agctgaggat gtccccaaga atacttggtta gctaagagaa 120
gaaaatggag ggatatatgt gatacttggt ttctttgatg ctggttgtaat tcttggtgatt 180
ttcatatatg tgaatacaag acttccacac catgcccttt ctttcgggat ctgtaaaatt 240
tagaagcttt aaaatgtata atgtacattt gttacatttc tgaacctttt tgctcatgct 300
ctttgttccc tgatgtagaa tggtcnattc tgtccgtcaa ggcccaacct gaatggtgtc 360
attaaatgtc aggcctttcc tcagtctctg ggggtctgaac tgctcagggg tcatcttgag 420
tcccggccat gcacctctgt ggaggccaaa gccacctccc tgatctctct aggtgccgct 480
cacggtgggt ttctcaatcg tcttcatgaa gttgagcctc atagaatggg gctgcccgct 540
ctgccggcag gtccatgagc tggagaagtc caagcggggc ctggagaccc agatggagga 600
gatgaagacg cagntggaag agctggagga cgagctgcaa gccacggagg acgccaaact 660
gcggctggaa gtcaacatgc aggcgctcaa gggccagttc gaaagggatc tccaagcccc 720
ggacgagcag aatgaggaga agag                                     744

```

<210> 130

<211> 29

<212> PRT

<213> Homo sapiens

<400> 130

```

Arg Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Glu
  1                      5                      10                      15

```


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Leu Leu Gln Glu Glu Thr Arg Gln Lys Leu Asn Val Ser
 20 25

<210> 131

<211> 89

<212> DNA

<213> Homo sapiens

<400> 131

acgcgaattt gaagatagag acaggtctca tcgggaggaa atggaggagc tgcttcaaga 60
 agaaaccggg cagaagctca acgtgtcta 89

<210> 132

<211> 452

<212> PRT

<213> Homo sapiens

<400> 132

Met Ser Glu Thr Pro Ala Gln Cys Ser Ile Lys Gln Glu Arg Ile Ser
 1 5 10 15

Tyr Thr Pro Pro Glu Ser Pro Val Pro Ser Tyr Ala Ser Ser Thr Pro
 20 25 30

Leu His Val Pro Val Pro Arg Ala Leu Arg Met Glu Glu Asp Ser Ile
 35 40 45

Arg Leu Pro Ala His Leu Arg Leu Gln Pro Ile Tyr Trp Ser Arg Asp
 50 55 60

Asp Val Ala Gln Trp Leu Lys Trp Ala Glu Asn Glu Phe Ser Leu Arg
 65 70 75 80

Pro Ile Asp Ser Asn Thr Phe Glu Met Asn Gly Lys Ala Leu Leu Leu
 85 90 95

Leu Thr Lys Glu Asp Phe Arg Tyr Arg Ser Pro His Ser Gly Asp Val
 100 105 110

Leu Tyr Glu Leu Leu Gln His Ile Leu Lys Gln Arg Lys Pro Arg Ile
 115 120 125

Leu Phe Ser Pro Phe Phe His Pro Gly Asn Ser Ile His Thr Gln Pro
 130 135 140

Glu Val Ile Leu His Gln Asn His Glu Glu Asp Asn Cys Val Gln Arg
 145 150 155 160

Thr Pro Arg Pro Ser Val Asp Asn Val His His Asn Pro Pro Thr Ile
 165 170 175

Glu Leu Leu His Arg Ser Arg Ser Pro Ile Thr Thr Asn His Arg Pro
 180 185 190

Ser Pro Asp Pro Glu Gln Arg Pro Leu Arg Ser Pro Leu Asp Asn Met

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195	200	205
Ile Arg Arg Leu Ser Pro Ala Glu Arg Ala Gln Gly Pro Arg Pro His 210 215 220		
Gln Glu Asn Asn His Gln Glu Ser Tyr Pro Leu Ser Val Ser Pro Met 225 230 235 240		
Glu Asn Asn His Cys Pro Ala Ser Ser Glu Ser His Pro Lys Pro Ser 245 250 255		
Ser Pro Arg Gln Glu Ser Thr Arg Val Ile Gln Leu Met Pro Ser Pro 260 265 270		
Ile Met His Pro Leu Ile Leu Asn Pro Arg His Ser Val Asp Phe Lys 275 280 285		
Gln Ser Arg Leu Ser Glu Asp Gly Leu His Arg Glu Gly Lys Pro Ile 290 295 300		
Asn Leu Ser His Arg Glu Asp Leu Ala Tyr Met Asn His Ile Met Val 305 310 315 320		
Ser Val Ser Pro Pro Glu Glu His Ala Met Pro Ile Gly Arg Ile Ala 325 330 335		
Asp Cys Arg Leu Leu Trp Asp Tyr Val Tyr Gln Leu Leu Ser Asp Ser 340 345 350		
Arg Tyr Glu Asn Phe Ile Arg Trp Glu Asp Lys Glu Ser Lys Ile Phe 355 360 365		
Arg Ile Val Asp Pro Asn Gly Leu Ala Arg Leu Trp Gly Asn His Lys 370 375 380		
Asn Arg Thr Asn Met Thr Tyr Glu Lys Met Ser Arg Ala Leu Arg His 385 390 395 400		
Tyr Tyr Lys Leu Asn Ile Ile Arg Lys Glu Pro Gly Gln Arg Leu Leu 405 410 415		
Phe Arg Phe Met Lys Thr Pro Asp Glu Ile Met Ser Gly Arg Thr Asp 420 425 430		
Arg Leu Glu His Leu Glu Ser Gln Glu Leu Asp Glu Gln Ile Tyr Gln 435 440 445		
Glu Asp Glu Cys 450		

<210> 133

<211> 1956

<212> DNA

<213> Homo sapiens

<400> 133

tcctgatctc tctcgctgtg agacatgtct gagactoctg ctcagtgtag cattaagcag 60

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gaacgaattt catatacacc tccagagagc ccagtgccga gttacgcttc ctcgacgcca 120
cttcatgttc cagtgcctcg agcgctcagg atggaggaag actcgatccg cctgcctgcg 180
cacctgcgct tgcagccaat ttactggagc agggatgacg tagcccagtg gctcaagtgg 240
gctgaaaatg agttttcttt aaggccaatt gacagcaaca cgtttgaaat gaatggcaaa 300
gctctcctgc tgcagaccaa agaggacttt cgctatcgat ctctcattc aggtgatgtg 360
ctctatgaac tccttcagca tattctgaag cagaggaaac ctcggtattct tttttcacca 420
ttcttcacc ctggaaactc tatacacaca cagccggagg tcatactgca tcagaaccat 480
gaagaagata actgtgtoca gaggaccccc aggccatccg tggataatgt gcaccataac 540
cctcccacca ttgaactggt gcaccgctcc aggtcaccta tcacgacaaa tcaccggcct 600
tctcctgacc ccgagcagcg gcccctccgg tccccctgg acaacatgat ccgcccgcctc 660
tccccggctg agagagctca gggacccagg ccgcaccagg agaacaacca ccaggagtcc 720
taccctctgt cagtgtctcc catggagaat aatcactgcc cagcgctctc caggtcccac 780
ccgaagccat ccagcccccg gcaggagagc acacgcgtga tccagctgat gccagcccc 840
atcatgcacc ctctgatcct gaaccccccg cactccgtgg atttcaaaca gtccaggctc 900
tccgaggacg ggctgcatag ggaagggaag cccatcaacc tctctcatcg ggaagacctg 960
gcttacatga accacatcat ggtctctgtc tccccgcctg aagagcacgc catgcccatt 1020
gggagaatag cagactgtag actgctttgg gattacgtct atcagttgct ttctgacagc 1080
cggtagcaaa acttcatccg atgggaggagc aaagaatcca aaatattccg gatagtggat 1140
cccaacggac tggctcgact gtggggaaac cataagaaca gaacaaacat gacctatgag 1200
aaaatgtcca gagccctgcg ccactactac aaactaaaca ttatcaggaa ggagccagga 1260
caaaggcttt tgttcagggt tatgaaaacc ccagatgaaa tcatgagtgg ccgaacagac 1320
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tgaaggaacc aacagtccac ctacgcgggc cagcagccca gggaaccct gccaccagg 1440
attgctggaa gtgtgacgga gcaggcgggc tgaggagagt ggaaaaggaa ggcaccaga 1500
aatggcaggg acacttctct tgcagaccaa gaggaccct ggagcacctt agacaaacta 1560
cccagcacag gcggggctgg aattctggcg gatggcacga gcctgggact ccatgtcacg 1620
tttccttctg atttggaatc tctccatctg taattcctca ccctcaccct tccaccgttg 1680
ttagtatcat ggtgtttttg tttttgtttt tgttttaaga acctgcagtt tgactcttca 1740
tcgttcatct aggggaagac atctgatgtt gttttcctat ggaaatatat atctattata 1800
tatatatatt ttttgcaaat ctcacaaagt gcggcaagcc cagctgggtca ggaaagagaa 1860
tacttgcaaa ggggttcagg ttctcttttt tcttgccacg tggatcaggt ctgttctgtg 1920
tactgttggg tcttggctga aaaaaaaaaa aaaaaa 1956

```

<210> 134

<211> 452

<212> PRT

<213> Homo sapiens

<400> 134

```

Met Ser Glu Thr Pro Ala Gln Cys Ser Ile Lys Gln Glu Arg Ile Ser
  1                      5                      10                      15

```

```

Tyr Thr Pro Pro Glu Ser Pro Val Pro Ser Tyr Ala Ser Ser Thr Pro
          20                      25                      30

```

```

Leu His Val Pro Val Pro Arg Ala Leu Arg Met Glu Glu Asp Ser Ile
          35                      40                      45

```

```

Arg Leu Pro Ala His Leu Arg Leu Gln Pro Ile Tyr Trp Ser Arg Asp
          50                      55                      60

```

```

Asp Val Ala Gln Trp Leu Lys Trp Ala Glu Asn Glu Phe Ser Leu Arg
          65                      70                      75                      80

```

```

Pro Ile Asp Ser Asn Thr Phe Glu Met Asn Gly Lys Ala Leu Leu Leu
          85                      90                      95

```

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Leu	Thr	Lys	Glu	Asp	Phe	Arg	Tyr	Arg	Ser	Pro	His	Ser	Gly	Asp	Val	100	105	110
Leu	Tyr	Glu	Leu	Leu	Gln	His	Ile	Leu	Lys	Gln	Arg	Lys	Pro	Arg	Ile	115	120	125
Leu	Phe	Ser	Pro	Phe	Phe	His	Pro	Gly	Asn	Ser	Ile	His	Thr	Gln	Pro	130	135	140
Glu	Val	Ile	Leu	His	Gln	Asn	His	Glu	Glu	Asp	Asn	Cys	Val	Gln	Arg	145	150	155
Thr	Pro	Arg	Pro	Ser	Val	Asp	Asn	Val	His	His	Asn	Pro	Pro	Thr	Ile	165	170	175
Glu	Leu	Leu	His	Arg	Ser	Arg	Ser	Pro	Ile	Thr	Thr	Asn	His	Arg	Pro	180	185	190
Ser	Pro	Asp	Pro	Glu	Gln	Arg	Pro	Leu	Arg	Ser	Pro	Leu	Asp	Asn	Met	195	200	205
Ile	Arg	Arg	Leu	Ser	Pro	Ala	Glu	Arg	Ala	Gln	Gly	Pro	Arg	Pro	His	210	215	220
Gln	Glu	Asn	Asn	His	Gln	Glu	Ser	Tyr	Pro	Leu	Ser	Val	Ser	Pro	Met	225	230	235
Glu	Asn	Asn	His	Cys	Pro	Ala	Ser	Ser	Glu	Ser	His	Pro	Lys	Pro	Ser	245	250	255
Ser	Pro	Arg	Gln	Glu	Ser	Thr	Arg	Val	Ile	Gln	Leu	Met	Pro	Ser	Pro	260	265	270
Ile	Met	His	Pro	Leu	Ile	Leu	Asn	Pro	Arg	His	Ser	Val	Asp	Phe	Lys	275	280	285
Gln	Ser	Arg	Leu	Ser	Glu	Asp	Gly	Leu	His	Arg	Glu	Gly	Lys	Pro	Ile	290	295	300
Asn	Leu	Ser	His	Arg	Glu	Asp	Leu	Ala	Tyr	Met	Asn	His	Ile	Met	Val	305	310	315
Ser	Val	Ser	Pro	Pro	Glu	Glu	His	Ala	Met	Pro	Ile	Gly	Arg	Ile	Ala	325	330	335
Asp	Cys	Arg	Leu	Leu	Trp	Asp	Tyr	Val	Tyr	Gln	Leu	Leu	Ser	Asp	Ser	340	345	350
Arg	Tyr	Glu	Asn	Phe	Ile	Arg	Trp	Glu	Asp	Lys	Glu	Ser	Lys	Ile	Phe	355	360	365
Arg	Ile	Val	Asp	Pro	Asn	Gly	Leu	Ala	Arg	Leu	Trp	Gly	Asn	His	Lys	370	375	380
Asn	Arg	Thr	Asn	Met	Thr	Tyr	Glu	Lys	Met	Ser	Arg	Ala	Leu	Arg	His	385	390	395
Tyr	Tyr	Lys	Leu	Asn	Ile	Ile	Arg	Lys	Glu	Pro	Gly	Gln	Arg	Leu	Leu			

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405	410	415
Phe Arg Phe Met Lys Thr Pro Asp	Glu Ile Met Ser Gly Arg Thr Asp	
420	425	430
Arg Leu Glu His Leu Glu Ser Gln	Glu Leu Asp Glu Gln Ile Tyr Gln	
435	440	445
Glu Asp Glu Cys		
450		

<210> 135
 <211> 1580
 <212> DNA
 <213> Homo sapiens

<400> 135

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cttcatgttc	cagtgcctcg	agcgctcagc	atggaggaag	actcgatccg	cctgcctgcg	180
cacctgcgct	tgcagccaat	ttactggagc	agggatgacg	tagcccagtg	gctcaagtgg	240
gctgaaaatg	agttttcttt	aaggccaatt	gacagcaaca	cgtttgaaat	gaatggcaaa	300
gctctcctgc	tgctgaccaa	agaggacttt	cgctatcgat	ctcctcattc	aggtgatgtg	360
ctctatgaac	tccttcagca	tattctgaag	cagaggaaac	ctcggattct	tttttcacca	420
ttcttccacc	ctggaaactc	tatacacaca	cagccggagg	tcatactgca	tcagaaccat	480
gaagaagata	actgtgtcca	gaggaccccc	aggccatccg	tggataatgt	gcaccataac	540
cctcccacca	ttgaactggt	gcaccgctcc	aggtcaccta	tcacgacaaa	tcaccggcct	600
tctcctgacc	ccgagcagcg	gccccctcgg	tcccccttgg	acaacatgat	ccgccgcctc	660
tccccggctg	agagagctca	gggacccagg	cgcaccagg	agaacaacca	ccaggagtcc	720
taccctctgt	cagtgtctcc	catggagaat	aatcactgcc	cagcgtcctc	cgagtcccac	780
ccgaagccat	ccagcccccg	gcaggagagc	acacgcgtga	tccagctgat	gcccagcccc	840
atcatgcacc	ctctgatcct	gaaccccccg	cactccgtgg	atttcaaaca	gtccaggctc	900
tccgaggacg	ggctgcatag	ggaaggggaag	cccatcaacc	tctctcatcg	ggaagacctg	960
gcttacatga	accacatcat	ggtctctgtc	tccccgcctg	aagagcacgc	catgcccatt	1020
gggagaatag	cagactgtag	actgcttttg	gattacgtct	atcagttgct	ttctgacagc	1080
cggtacgaaa	acttcatccg	atgggaggac	aaagaatcca	aaatattccg	gatagtggat	1140
cccaacggac	tggtctgact	gtggggaaac	cataagaaca	gaacaaacat	gacctatgag	1200
aaaatgtcca	gagccctgcg	ccactactac	aaactaaaaca	ttatcaggaa	ggagccagga	1260
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<210> 136
 <211> 1451
 <212> DNA
 <213> Homo sapiens

<400> 136

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ggtgccaaag	tgctacttcg	ttatgctagt	ccctggaatt	gggtgggggtg	gtgattaggg	180
cagcccaggc	caagccaaaa	cggaaagctcc	caaccttccc	cccaccagag	cagctgcagt	240
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gggtggggag ctccttcagt gtccatcacg atgggtgaaag ctgcggcccca cccctagacg 360
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gaaaatcggg ttctgagtat atttctgttc agcctgtgag ccaagggtgag ctgacctgca 540
ggtcacagag aactcagtgt ggtcccaacc agctcttact gctggcagag acatgccag 600
gacagatggg cagaggcttg aaaagggcag agggaaaggc tcttgagagc cctcgaggc 660
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<210> 137

<211> 1565

<212> DNA

<213> Homo sapiens

<400> 137

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agtttgtcct ctttagtgca gttgcttggt tcccagtttg gacttaaagc atgggtatag 180
tactactgtc tttttaatag gttccaatgt gagtctagaa attggagagg acaataaat 240
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<210> 138

110/299

<211> 1679

<212> DNA

<213> Homo sapiens

<400> 138

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tactactgtc tttttaatag gttccaatgt gagtctagaa attggagagg acaaataaat 240
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<210> 139

<211> 680

<212> PRT

<213> Homo sapiens

<400> 139

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Tyr Leu Phe Gly Cys Glu Leu Lys Ala Asp Lys Asp Tyr His Phe Lys
          20                      25                      30

Val Asp Asn Asp Glu Asn Glu His Gln Leu Ser Leu Arg Thr Val Ser
          35                      40                      45

Leu Gly Ala Gly Ala Lys Asp Glu Leu His Ile Val Glu Ala Glu Ala
          50                      55                      60

Met Asn Tyr Glu Gly Ser Pro Ile Lys Val Thr Leu Ala Thr Leu Lys
          65                      70                      75                      80

Met Ser Val Gln Pro Thr Val Ser Leu Gly Gly Phe Glu Ile Thr Pro
          85                      90                      95

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Pro Val Val Leu Arg Leu Lys Cys Gly Ser Gly Pro Val His Ile Ser
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 Gly Gln His Leu Val Val Tyr Arg Arg Lys His Gln Glu Leu Gln Ala
 115 120 125
 Met Gln Met Glu Leu Gln Ser Pro Glu Tyr Lys Leu Ser Lys Leu Arg
 130 135 140
 Thr Ser Thr Ile Met Thr Asp Tyr Asn Pro Asn Tyr Cys Phe Ala Gly
 145 150 155 160
 Lys Thr Ser Ser Ile Ser Asp Leu Lys Glu Val Pro Arg Lys Asn Ile
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 Thr Leu Ile Arg Gly Leu Gly His Gly Ala Phe Gly Glu Val Tyr Glu
 180 185 190
 Gly Gln Val Ser Gly Met Pro Asn Asp Pro Ser Pro Leu Gln Val Ala
 195 200 205
 Val Lys Thr Leu Pro Glu Val Cys Ser Glu Gln Asp Glu Leu Asp Phe
 210 215 220
 Leu Met Glu Ala Leu Ile Ile Ser Lys Phe Asn His Gln Asn Ile Val
 225 230 235 240
 Arg Cys Ile Gly Val Ser Leu Gln Ser Leu Pro Arg Phe Ile Leu Leu
 245 250 255
 Glu Leu Met Ala Gly Gly Asp Leu Lys Ser Phe Leu Arg Glu Thr Arg
 260 265 270
 Pro Arg Pro Ser Gln Pro Ser Ser Leu Ala Met Leu Asp Leu Leu His
 275 280 285
 Val Ala Arg Asp Ile Ala Cys Gly Cys Gln Tyr Leu Glu Glu Asn His
 290 295 300
 Phe Ile His Arg Asp Ile Ala Ala Arg Asn Cys Leu Leu Thr Cys Pro
 305 310 315 320
 Gly Pro Gly Arg Val Ala Lys Ile Gly Asp Phe Gly Met Ala Arg Asp
 325 330 335
 Ile Tyr Arg Ala Ser Tyr Tyr Arg Lys Gly Gly Cys Ala Met Leu Pro
 340 345 350
 Val Lys Trp Met Pro Pro Glu Ala Phe Met Glu Gly Ile Phe Thr Ser
 355 360 365
 Lys Thr Asp Thr Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Ser
 370 375 380
 Leu Gly Tyr Met Pro Tyr Pro Ser Lys Ser Asn Gln Glu Val Leu Glu
 385 390 395 400

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Phe Val Thr Ser Gly Gly Arg Met Asp Pro Pro Lys Asn Cys Pro Gly
 405 410 415
 Pro Val Tyr Arg Ile Met Thr Gln Cys Trp Gln His Gln Pro Glu Asp
 420 425 430
 Arg Pro Asn Phe Ala Ile Ile Leu Glu Arg Ile Glu Tyr Cys Thr Gln
 435 440 445
 Asp Pro Asp Val Ile Asn Thr Ala Leu Pro Ile Glu Tyr Gly Pro Leu
 450 455 460
 Val Glu Glu Glu Glu Lys Val Pro Val Arg Pro Lys Asp Pro Glu Gly
 465 470 475 480
 Val Pro Pro Leu Leu Val Ser Gln Gln Ala Lys Arg Glu Glu Glu Arg
 485 490 495
 Ser Pro Ala Ala Pro Pro Pro Leu Pro Thr Thr Ser Ser Gly Lys Ala
 500 505 510
 Ala Lys Lys Pro Thr Ala Ala Glu Val Ser Val Arg Val Pro Arg Gly
 515 520 525
 Pro Ala Val Glu Gly Gly His Val Asn Met Ala Phe Ser Gln Ser Asn
 530 535 540
 Pro Pro Ser Glu Leu His Lys Val His Gly Ser Arg Asn Lys Pro Thr
 545 550 555 560
 Ser Leu Trp Asn Pro Thr Tyr Gly Ser Trp Phe Thr Glu Lys Pro Thr
 565 570 575
 Lys Lys Asn Asn Pro Ile Ala Lys Lys Glu Pro His Asp Arg Gly Asn
 580 585 590
 Leu Gly Leu Glu Gly Ser Cys Thr Val Pro Pro Asn Val Ala Thr Gly
 595 600 605
 Arg Leu Pro Gly Ala Ser Leu Leu Leu Glu Pro Ser Ser Leu Thr Ala
 610 615 620
 Asn Met Lys Glu Val Pro Leu Phe Arg Leu Arg His Phe Pro Cys Gly
 625 630 635 640
 Asn Val Asn Tyr Gly Tyr Gln Gln Gln Gly Leu Pro Leu Glu Ala Ala
 645 650 655
 Thr Ala Pro Gly Ala Gly His Tyr Glu Asp Thr Ile Leu Lys Ser Lys
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<210> 140

<211> 2043

<212> DNA

113/299

<213> Homo sapiens

<400> 140

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aatgtcaatt acggctacca gcaacagggc ttgcccttag aagccgctac tgcccctgga 1980
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<210> 141

<211> 180

<212> DNA

<213> Homo sapiens

<400> 141

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<210> 142

<211> 180

<212> DNA

<213> Homo sapiens

<400> 142

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 tcctggagct taggatgtgt gatgcagaag aagtctggaa aggtaagaaa cagaattgta 180

<210> 143

<211> 427

<212> DNA

<213> Homo sapiens

<400> 143

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 aataaatcag agccctcaag acactgaatg ccaggagcat ggtctgaggg acagtgtgct 180
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<210> 144

<211> 438

<212> DNA

<213> Homo sapiens

<400> 144

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 atagtaggtg ctaaataaat atttgttgaa tggatgaatt gttaggtaag tagaaataga 180
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 ttgtatagat gaattgaatg gatggttgaa tggatggata gatggatgga tgggtggaat 360
 agatggatgg acggatggat ggatggatgg atggatggat ggatggatga tgkatggatg 420
 gacggacaga cggacgga 438

<210> 145

<211> 135

<212> DNA

<213> Homo sapiens

<400> 145

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 tacctcttcg gatga 135

<210> 146

<211> 476

<212> PRT

<213> Homo sapiens

<400> 146

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 Gly Tyr Ser Ala Tyr Thr Ala Gln Pro Thr Gln Gly Tyr Ala Gln Thr
 20 25 30

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Thr Gln Ala Tyr Gly Gln Gln Ser Tyr Gly Thr Tyr Gly Gln Pro Thr
 35 40 45
 Asp Val Ser Tyr Thr Gln Ala Gln Thr Thr Ala Thr Tyr Gly Gln Thr
 50 55 60
 Ala Tyr Ala Thr Ser Tyr Gly Gln Pro Pro Thr Gly Tyr Thr Thr Pro
 65 70 75 80
 Thr Ala Pro Gln Ala Tyr Ser Gln Pro Val Gln Gly Tyr Gly Thr Gly
 85 90 95
 Ala Tyr Asp Thr Thr Thr Ala Thr Val Thr Thr Thr Gln Ala Ser Tyr
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 Ala Ala Gln Ser Ala Tyr Gly Thr Gln Pro Ala Tyr Pro Ala Tyr Gly
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 Gln Gln Pro Ala Ala Thr Ala Pro Thr Arg Pro Gln Asp Gly Asn Lys
 130 135 140
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 Pro Ser Leu Gly Tyr Gly Gln Ser Asn Tyr Ser Tyr Pro Gln Val Pro
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 Gly Ser Tyr Pro Met Gln Pro Val Thr Ala Pro Pro Ser Tyr Pro Pro
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 Thr Ser Tyr Ser Ser Thr Gln Pro Thr Ser Tyr Asp Gln Ser Ser Tyr
 195 200 205
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 210 215 220
 Ser Tyr Gly Gln Gln Ser Ser Tyr Gly Gln Gln Pro Pro Thr Ser Tyr
 225 230 235 240
 Pro Pro Gln Thr Gly Ser Tyr Ser Gln Ala Pro Ser Gln Tyr Ser Gln
 245 250 255
 Gln Ser Ser Ser Tyr Gly Gln Gln Ser Pro Pro Leu Gly Gly Ala Gln
 260 265 270
 Thr Ile Ser Lys Asn Thr Glu Gln Arg Pro Gln Pro Asp Pro Tyr Gln
 275 280 285
 Ile Leu Gly Pro Thr Ser Ser Arg Leu Ala Asn Pro Gly Ser Gly Gln
 290 295 300
 Ile Gln Leu Trp Gln Phe Leu Leu Glu Leu Leu Ser Asp Ser Ala Asn
 305 310 315 320
 Ala Ser Cys Ile Thr Trp Glu Gly Thr Asn Gly Glu Phe Lys Met Thr
 325 330 335

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Asp Pro Asp Glu Val Ala Arg Arg Trp Gly Gln Arg Lys Ser Lys Pro
 340 345 350
 Asn Met Asn Tyr Asp Lys Leu Ser Arg Ala Leu Arg Tyr Tyr Tyr Asp
 355 360 365
 Lys Asn Ile Met Thr Lys Val His Gly Lys Arg Tyr Ala Tyr Lys Phe
 370 375 380
 Asp Phe His Gly Ile Ala Gln Ala Leu Gln Pro His Pro Thr Glu Ser
 385 390 395 400
 Ser Met Tyr Lys Tyr Pro Ser Asp Ile Ser Tyr Met Pro Ser Tyr His
 405 410 415
 Ala His Gln Gln Lys Val Asn Phe Val Pro Pro His Pro Ser Ser Met
 420 425 430
 Pro Val Thr Ser Ser Ser Phe Phe Gly Ala Ala Ser Gln Tyr Trp Thr
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<210> 147

<211> 1431

<212> DNA

<213> Homo sapiens

<400> 147

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tccatgtaca agtacccttc tgacatctcc tacatgcctt cctaccatgc ccaccagcag 1260
aaggtgaact ttgtccctcc ccatccatcc tccatgcctg tcacttcctc cagcttcttt 1320
ggagccgcat cacaatactg gacctcccc acggggggaa tctaccccaa cccaacgctc 1380
ccccgccatc ctaacaccca cgtgccttca cacttaggca gctactacta g 1431

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<210> 148
 <211> 154
 <212> PRT
 <213> Homo sapiens

<400> 148
 Met Asp Leu Pro Tyr Tyr His Gly Arg Leu Thr Lys Gln Asp Cys Glu
 1 5 10 15
 Thr Leu Leu Leu Lys Glu Gly Val Asp Gly Asn Phe Leu Leu Arg Asp
 20 25 30
 Ser Glu Ser Ile Pro Gly Val Leu Cys Leu Cys Val Ser Phe Lys Asn
 35 40 45
 Ile Val Tyr Thr Tyr Arg Ile Phe Arg Glu Lys His Gly Tyr Tyr Arg
 50 55 60
 Ile Gln Pro Ile Lys Arg Thr Ser Pro Ser Leu Arg Trp Arg Gly Ser
 65 70 75 80
 Lys Leu Glu Leu Glu Ala Phe Met Thr Ala Glu Gly Ser Pro Lys Gln
 85 90 95
 Val Phe Pro Ser Leu Lys Glu Leu Ile Ser Lys Phe Glu Lys Pro Asn
 100 105 110
 Gln Gly Met Val Val His Leu Leu Lys Pro Ile Lys Arg Thr Ser Pro
 115 120 125
 Ser Leu Arg Trp Arg Gly Leu Lys Leu Glu Leu Glu Thr Phe Val Asn
 130 135 140
 Ser Asn Ser Asp Tyr Val Asp Val Leu Pro
 145 150

<210> 149
 <211> 465
 <212> DNA
 <213> Homo sapiens

<400> 149
 atggatctgc cttactacca tggacgtctg accaagcaag actgtgagac cttgctgctc 60
 aaggaagggg tggatggcaa ctttctttta agagacagcg agtcgatacc aggagtcttg 120
 tgcctctgtg tctcgtttaa aaatattgtc tacacatacc gaatcttcag agagaaacac 180
 ggggtattaca ggatacagcc aataaagaga accagcccca gcttgagatg gagaggatcg 240
 aaattagagt tggaagcatt tatgactgca gaaggttctc caaaacaggt ctttccaagc 300
 ctaaaggaac tgatctccaa atttgaaaaa ccaaatacagg ggatgggtggg tcacctttta 360
 aagccaataa agagaaccag cccagcttg agatggagag gattgaaatt agagttggaa 420
 acatttgtga acagtaacag cgattatgtg gatgtcttgc cttga 465

<210> 150
 <211> 132
 <212> PRT

118/299

<213> Homo sapiens

<400> 150

Met Asp Leu Pro Tyr Tyr His Gly Arg Leu Thr Lys Gln Asp Cys Glu
 1 5 10 15

Thr Leu Leu Leu Lys Glu Gly Val Asp Gly Asn Phe Leu Leu Arg Asp
 20 25 30

Ser Glu Ser Ile Pro Gly Val Leu Cys Leu Cys Val Ser Phe Lys Asn
 35 40 45

Ile Val Tyr Thr Tyr Arg Ile Phe Arg Glu Lys His Gly Tyr Tyr Arg
 50 55 60

Ile Gln Thr Ala Glu Gly Ser Pro Lys Gln Val Phe Pro Ser Leu Lys
 65 70 75 80

Glu Leu Ile Ser Lys Phe Glu Lys Pro Asn Gln Gly Met Val Val His
 85 90 95

Leu Leu Lys Pro Ile Lys Arg Thr Ser Pro Ser Leu Arg Trp Arg Gly
 100 105 110

Leu Lys Leu Glu Leu Glu Thr Phe Val Asn Ser Asn Ser Asp Tyr Val
 115 120 125

Asp Val Leu Pro
 130

<210> 151

<211> 420

<212> DNA

<213> Homo sapiens

<400> 151

atggatctgc cttactacca tggacgtctg accaagcaag actgtgagac cttgctgctc 60
 aaggaagggg tggatggcaa ctttctttta agagacagcg agtcgatacc aggagtcctg 120
 tgcctctgtg tctcgtttta aaatattgtc tacacatacc gaatcttcag agagaaacac 180
 gggatttaca ggatacagac tgcagaaggt tctccaaaac aggtctttcc aagcctaaag 240
 gaactgatct ccaaatttga aaaaccaa at caggggatgg tggttcacct tttaaagcca 300
 ataaagagaa ccagccccag cttgagatgg agaggattga aattagagtt ggaaacattt 360
 gtgaacagta acagcgatta tgtggatgtc ttgccttgaa gataaggctg cggacaaaag 420

<210> 152

<211> 45

<212> PRT

<213> Homo sapiens

<400> 152

Met Asp Leu Pro Tyr Tyr His Gly Arg Leu Thr Lys Gln Asp Cys Glu
 1 5 10 15

Thr Leu Leu Leu Lys Glu Gly Val Asp Gly Asn Phe Leu Leu Arg Asp
 20 25 30

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Ser Glu Ser Ile Pro Gly Val Leu Cys Leu Cys Val Ser
 35 40 45

<210> 153
 <211> 136
 <212> DNA
 <213> Homo sapiens

<400> 153
 atggatctgc cttactacca tggacgtctg accaagcaag actgtgagac cttgctgctc 60
 aaggaagggg tggatggcaa ctttctttta agagacagcg agtcgatacc aggagtcctg 120
 tgcctctgtg tctcgt 136

<210> 154
 <211> 132
 <212> PRT
 <213> Mus musculus

<400> 154
 Met Asp Leu Pro Tyr Tyr His Gly Cys Leu Thr Lys Arg Glu Cys Glu
 1 5 10 15
 Ala Leu Leu Leu Lys Gly Gly Val Asp Gly Asn Phe Leu Ile Arg Asp
 20 25 30
 Ser Glu Ser Val Pro Gly Ala Leu Cys Leu Cys Val Ser Phe Lys Lys
 35 40 45
 Leu Val Tyr Ser Tyr Arg Ile Phe Arg Glu Lys His Gly Tyr Tyr Arg
 50 55 60
 Ile Glu Thr Asp Ala His Thr Pro Arg Thr Ile Phe Pro Asn Leu Gln
 65 70 75 80
 Glu Leu Val Ser Lys Tyr Gly Lys Pro Gly Gln Gly Leu Val Val His
 85 90 95
 Leu Ser Asn Pro Ile Met Arg Asn Asn Leu Cys Gln Arg Gly Arg Arg
 100 105 110
 Met Glu Leu Glu Leu Asn Val Tyr Glu Asn Thr Asp Glu Glu Tyr Val
 115 120 125
 Asp Val Leu Pro
 130

<210> 155
 <211> 399
 <212> DNA
 <213> Mus musculus

<400> 155
 atggatctgc cttactacca tggctgcctg accaagcgag agtgtgaagc cctgctcctc 60
 aagggaggtg tggatggcaa ctttctgata agagacagcg agtctgtgcc aggagccctg 120
 tgcctctgtg tctcgtttta aaagcttgtc tacagctacc gaatcttcag agagaaacat 180

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ggatattaca ggatagagac tgatgctcat actccaagaa cgatctttcc aaacctacag 240
gaattggtct ccaaatatgg aaaaccgggt caaggattgg tggttcacct ttcaaaccga 300
ataatgagaa acaacctatg ccaaagaggg agaagaatgg agttagagct gaatgtttat 360
gagaacactg atgaggagta tgtggacgtc ttgccttga 399

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<210> 156
 <211> 76
 <212> PRT
 <213> Homo sapiens

<400> 156
 Pro Thr Ser Tyr Pro Pro Gln Thr Gly Ser Tyr Ser Gln Ala Pro Ser
 1 5 10 15
 Gln Tyr Ser Gln Gln Ser Ser Ser Tyr Gly Gln Gln Asn Pro Tyr Gln
 20 25 30
 Ile Leu Gly Pro Thr Ser Ser Arg Leu Ala Asn Pro Gly Ser Gly Gln
 35 40 45
 Ile Gln Leu Trp Gln Phe Leu Leu Glu Leu Leu Ser Asp Ser Ala Asn
 50 55 60
 Ala Ser Cys Ile Thr Trp Glu Gly Thr Asn Gly Glu
 65 70 75

<210> 157
 <211> 229
 <212> DNA
 <213> Homo sapiens

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<400> 157
cccactagtt acccacccca aactggatcc tacagccaag ctccaagtca atatagccaa 60
cagagcagca gctacgggca gcagaatccg tatcagatcc tgggcccgcag cagcagtcgc 120
ctagccaacc ctggaagcgg gcagatccag ctgtggcaat tcctcctgga gctgctctcc 180
gacagcgcca acgccagctg tatcacctgg gaggggacca acggggagt 229

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<210> 158
 <211> 100
 <212> DNA
 <213> Homo sapiens

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<400> 158
tacgggcagc agagttcact gctggcctat aatacaacct cccacaccga ccaatcctca 60
cgattgagtg tcaaagaaga cccttcttat gactcagtca 100

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<210> 159
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 159
 Ser Gln Gln Ser Ser Ser Tyr Gly Gln Gln Ser Pro Pro Leu Gly Gly
 1 5 10 15

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Ala Gln Thr Ile
20

<210> 160
<211> 60
<212> DNA
<213> Homo sapiens

<400> 160
agccaacaga gcagcagcta cgggcagcag agtcctcccc ttggaggggc acaaacgata 60

<210> 161
<211> 447
<212> DNA
<213> Homo sapiens

<400> 161
agatagagct ggagacctac aaactgaagt gcaaggcact gcaggaggag aaccgcgacc 60
tgcgcaaagc cagcgttacc atcatactgg agaacaggcc atctgttctg tttctacctg 120
tcccctggag gctgcccaga aaccggccct cgctggactc catggagAAC cagggtctccg 180
tggatgcctt caagatcctg gaggatccaa agtgggaatt ccctcggaag aacttggttc 240
ttggaaaaac tctaggagaa ggcgaatttg gaaaagtggc caaggcaacg gccttccatc 300
tgaaaggcag agcagggtac accacgggtg ccgtgaagat gctgaaagag aacgcctccc 360
cgagtgaagt tgcagacctg ctgtcagagt tcaacgtcct gaagcaggtc aaccacccac 420
atgtcatcaa attgtatggg gcctgca 447

<210> 162
<211> 585
<212> PRT
<213> Homo sapiens

<400> 162
Met Ala Asp Ser Ala Ser Glu Ser Asp Thr Asp Gly Ala Gly Gly Asn
1 5 10 15
Ser Ser Ser Ser Ala Ala Met Gln Ser Ser Cys Ser Ser Thr Ser Gly
20 25 30
Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Lys Ser Gly Gly
35 40 45
Ile Val Ile Ser Pro Phe Arg Leu Glu Glu Leu Thr Asn Arg Leu Ala
50 55 60
Ser Leu Gln Gln Glu Asn Lys Val Leu Lys Ile Glu Leu Glu Thr Tyr
65 70 75 80
Lys Leu Lys Cys Lys Ala Leu Gln Glu Glu Asn Arg Asp Leu Arg Lys
85 90 95
Ala Ser Val Thr Ile Gln Ala Arg Ala Glu Gln Glu Glu Glu Phe Ile
100 105 110
Ser Asn Thr Leu Phe Lys Lys Ile Gln Ala Leu Gln Lys Glu Lys Glu

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115					120					125					
Thr	Leu	Ala	Val	Asn	Tyr	Glu	Lys	Glu	Glu	Glu	Phe	Leu	Thr	Asn	Glu
130						135					140				
Leu	Ser	Arg	Lys	Leu	Met	Gln	Leu	Gln	His	Glu	Lys	Gly	Glu	Leu	Glu
145					150					155					160
Gln	His	Leu	Glu	Gln	Glu	Gln	Glu	Phe	Gln	Val	Asn	Lys	Leu	Met	Lys
				165					170					175	
Lys	Ile	Lys	Lys	Leu	Glu	Asn	Asp	Thr	Ile	Ser	Lys	Gln	Leu	Thr	Leu
			180					185					190		
Glu	Gln	Leu	Arg	Arg	Glu	Lys	Ile	Asp	Leu	Glu	Asn	Thr	Leu	Glu	Gln
		195					200					205			
Glu	Gln	Glu	Ala	Leu	Val	Asn	Arg	Leu	Trp	Lys	Arg	Met	Asp	Lys	Leu
		210				215					220				
Glu	Ala	Glu	Thr	Arg	Ile	Leu	Gln	Glu	Lys	Leu	Asp	Gln	Pro	Val	Ser
225					230					235					240
Ala	Pro	Pro	Ser	Pro	Arg	Asp	Ile	Ser	Met	Glu	Ile	Asp	Ser	Pro	Glu
				245					250					255	
Asn	Met	Met	Arg	His	Ile	Arg	Phe	Leu	Lys	Asn	Glu	Val	Glu	Arg	Leu
			260					265					270		
Lys	Lys	Gln	Leu	Arg	Ala	Ala	Gln	Leu	Gln	His	Ser	Glu	Lys	Met	Ala
		275					280					285			
Gln	Tyr	Leu	Glu	Glu	Glu	Arg	His	Met	Arg	Glu	Glu	Asn	Leu	Arg	Leu
	290					295						300			
Gln	Arg	Lys	Leu	Gln	Arg	Glu	Met	Glu	Arg	Arg	Glu	Ala	Leu	Cys	Arg
305					310					315					320
Gln	Leu	Ser	Glu	Ser	Glu	Ser	Ser	Leu	Glu	Met	Asp	Asp	Glu	Arg	Tyr
				325					330					335	
Phe	Asn	Glu	Met	Ser	Ala	Gln	Gly	Leu	Arg	Pro	Arg	Thr	Val	Ser	Ser
			340					345					350		
Pro	Ile	Pro	Tyr	Thr	Pro	Ser	Pro	Ser	Ser	Ser	Arg	Pro	Ile	Ser	Pro
		355					360					365			
Gly	Leu	Ser	Tyr	Ala	Ser	His	Thr	Val	Gly	Phe	Thr	Pro	Pro	Thr	Ser
	370					375					380				
Leu	Thr	Arg	Ala	Gly	Met	Ser	Tyr	Tyr	Asn	Ser	Pro	Gly	Leu	His	Val
385					390					395					400
Gln	His	Met	Gly	Thr	Ser	His	Gly	Ile	Thr	Arg	Pro	Ser	Pro	Arg	Arg
				405					410					415	
Ser	Asn	Ser	Pro	Asp	Lys	Phe	Lys	Arg	Pro	Thr	Pro	Pro	Pro	Ser	Pro
			420					425					430		

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Asn Thr Gln Thr Pro Val Gln Pro Pro Pro Pro Pro Pro Pro Pro Pro
 435 440 445

Met Gln Pro Thr Val Pro Ser Gly Ser His Leu Ala Ala Tyr Ser Phe
 450 455 460

Ala Thr Phe Gly Ala His Leu Leu Pro Ala Leu Met His Glu Leu Ser
 465 470 475 480

Leu Asn Phe Lys Leu Gly Leu Ile Gln Trp Ser Arg Leu Leu Asn Ala
 485 490 495

Lys Gly Ser Phe Ser Gly Ile Phe Gly Tyr Asp Leu Phe Ala Leu Arg
 500 505 510

Leu Ser Arg Leu His Tyr Pro Leu Cys Cys Lys Cys Leu Ser Glu Met
 515 520 525

Gln Pro Val Leu Trp Val Tyr Asn Thr Asn Gln Thr Thr Phe Ser Ile
 530 535 540

Ser Val Leu Leu Glu Ser Ser Cys Thr Ser Ile Pro Trp Leu Glu Pro
 545 550 555 560

Ser Leu Phe Gly Ile Trp Tyr Phe Ser Ser Ser Val Gln Phe Leu Leu
 565 570 575

Gly Pro Glu Leu His Ser Pro Gly Phe
 580 585

<210> 163

<211> 3011

<212> DNA

<213> Homo sapiens

<400> 163

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ctgctgctcc tcttcctttc ccagcccgcc gcggccatgg cggacagcgc cagcgagagc 60
gacacggacg gggcgggggg caacagcagc agctcgggccg ccatgcagtc gtcctgctcg 120
tcgacctcgg gcggcgggcg tggcgggcggg ggaggcgggc gcggtgggaa gtcggggggc 180
attgtcatct cgccgttccg cctggaggag ctcaccaacc gcctggcctc gctgcagcaa 240
gagaacaagg tgctgaagat agagctggag acctacaaac tgaagtgcaa ggcactgcag 300
gaggagaacc gcgacctgcg caaagccagc gttaccatcc aagccagggc tgagcaggaa 360
gaagaattca ttagtaacac ttatttcaag aaaattcagg ctttgcagaa ggagaaagaa 420
acccttgctg taaattatga gaaagaagaa gaattcctca ctaatgagct ctccagaaaa 480
ttgatgcagt tgcagcatga gaaaggcgaa ctagaacagc atcttgaaca agagcaggaa 540
tttcaggtca acaaaactgat gaagaaaatt aaaaaactgg agaatgacac catttctaag 600
caacttacat tagaacagtt gagacgggag aagattgacc ttgaaaatac attggaacaa 660
gaacaagaag cactagttaa tcgcctctgg aaaaggatgg ataagcttga agctgaaacg 720
cgaatcctgc aggaaaaatt agaccagccc gtctctgctc caccatcgcc tagagatatc 780
tccatggaga ttgattctcc agaaaatatg atgcgtcaca tcagggtttt aaagaatgaa 840
gtggaacggc tgaagaagca actgagagct gctcagttac agcattcaga gaaaatggca 900
cagtatctgg aggaggaacg tcacatgaga gaagagaact tgaggctcca gaggaagctg 960
cagagggaga tggagagacg agaagccctc tgtcgacagc tctccgagag tagtccagc 1020
ttagaaatgg acgacgaaag gtattttaat gagatgtctg cacaaggatt aagacctcga 1080
actgtgtcca gcccgatccc ttacacacct tctccgagtt caagcaggcc tatatcacct 1140
ggtctatcat atgcaagtca cacggttggg ttcacgccac caacttcact gactagagct 1200

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ggaatgtctt attacaattc cccgggtctt cactgtgcagc acatgggaac atcccatggt 1260
atcacaaaggc cttcaccacg gagaagcaac agtcctgaca aattcaaacg gcccacgccc 1320
cctccatctc ccaacacaca gaccccagtc cagccacctc cacctccacc tccggccacc 1380
atgcagccca cgggtccctc aggcagccac ctgcagacct actccttcgc aacattcggc 1440
gcacacctcc tcccagcctt aatgcatgag cttagtctga atttcaagtt gggactcatc 1500
caatggagcc gtctactcaa cgccaaaggt tccttctctg gcataatttg atattgactta 1560
tttgactga ggttatctag gcttcactat ccattgtgtt gtaaattgtt gtcagaaatg 1620
cagccagtggt tgtgggtcta caacactaac cagacgactt tttccatcag tgttttactt 1680
gaatcttcat gtacgtccat tccctggctg gaaccttcgc tgtttgggtat ttggtatttc 1740
agcagcagtg tgcaattttt gcttggccca gagcttcatt ctcttggtt ttaggtttgt 1800
aaaagaaaaa gggatatctt ttttatattt ttttccatga atctgcagaa aataactaag 1860
ctgttgtaac cctcctataa ttataatagt gtttacaac aataccaata attcagcact 1920
acaattcaga cctttgaaaa tctggctttc agtgtagaac agaaagttag atgaatcagt 1980
gcccagaca tatttcctgt ttaacagaac tttctacaga tacatttttt acaggttatt 2040
ttcatttgtt tattgacatc catgtctctc gtaaacagag gtcccaaagt aatgaatcat 2100
gtggcgtagc ttctccacat aaatggatgg ataattacgt atattaagat gtgattctct 2160
tttttatcct taatgttaat ctacttaacc tggccccctc taacatgagt cgataaatgt 2220
tgtcctactc accggtggtt tcaatggcta attagaatgt gttattttgat ttctgctgca 2280
gaaggcagtg tgattgtaac aaaaacaatg cggcttcccc ctttcgtact tcatttgtgt 2340
tctcttaaaa tagagtttga acaaataatt taaagggtgca aaataccatt agaaaatact 2400
atttgaatg gacattatcg cattatcttg gcataatggc cagaaaatat tgtattgctt 2460
ggcagaaaaa gaaaaaaggt ctaaaggaaa gtagcacatt agcattgatg gctgttcatt 2520
tcaccagta taagcaagt tacaagaag tatattctga atacattatt tccattcatt 2580
tagcacaaat aaatcatttg gtttcacttt gcagtggaa actgagtcac tcttttctta 2640
atacgtgcaa catcttaatt tttgtttttc agcagttgct gttttgtact ttggtagtga 2700
agtgattttt accacctgtg tttgcatatt tatatatgct gtggatgaaa ataacttact 2760
agagaatgta tattttatga caagaatgtg tatctgttgg gatataatca gagaactgaa 2820
aagtaattta tcagtaattt ttaagagtcc atgttttgtg acaaccatct ctaatagcca 2880
actctttatt aaacacactc ctaaaaataa ggaaccatga cgattgtaga tatttaatat 2940
tgtacagtat agaaacctcc gatttttgcc ttcgaatgca gtatttaaga gttaacagaa 3000
aaaaaaaaa a 3011

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<210> 164
 <211> 447
 <212> DNA
 <213> Homo sapiens

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<400> 164
gatcaggggg ctcggaggcc ctcccttggg acacgtgtgg ctggcgagct ggtgggtgagg 60
gggcagtcct tggctttccc gcaccgcag tgccctgcgg ttcccagccc gcccgtgggtc 120
accagacggc ggcggggcggg tcccggagct ttccagccagc tttgctgggc ggcctaggga 180
gcgcgcccag cccggctgga gcgagcccca gtgcaatact gcccaagccc gggcgggggtc 240
tctgttctct ggcagaggag gtcccttggc agcgggaggc gccctctctt tctctcgccg 300
ccgctccgag tctgcgccct ggtgccagge gctcagctcg gcgctcccct gtgctcgccc 360
ggcggccact cattcgagc cgggccttcg tcgcgcgcgc ctccctgctg ctccctctcc 420
tttcccagc cgcgcgcgc catggcg 447

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<210> 165
 <211> 585
 <212> PRT
 <213> Homo sapiens

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<400> 165
Met Ala Asp Ser Ala Ser Glu Ser Asp Thr Asp Gly Ala Gly Gly Asn
  1             5             10             15

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Ser Ser Ser Ser Ala Ala Met Gln Ser Ser Cys Ser Ser Thr Ser Gly
 20 25 30
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Lys Ser Gly Gly
 35 40 45
 Ile Val Ile Ser Pro Phe Arg Leu Glu Glu Leu Thr Asn Arg Leu Ala
 50 55 60
 Ser Leu Gln Gln Glu Asn Lys Val Leu Lys Ile Glu Leu Glu Thr Tyr
 65 70 75 80
 Lys Leu Lys Cys Lys Ala Leu Gln Glu Glu Asn Arg Asp Leu Arg Lys
 85 90 95
 Ala Ser Val Thr Ile Gln Ala Arg Ala Glu Gln Glu Glu Glu Phe Ile
 100 105 110
 Ser Asn Thr Leu Phe Lys Lys Ile Gln Ala Leu Gln Lys Glu Lys Glu
 115 120 125
 Thr Leu Ala Val Asn Tyr Glu Lys Glu Glu Glu Phe Leu Thr Asn Glu
 130 135 140
 Leu Ser Arg Lys Leu Met Gln Leu Gln His Glu Lys Gly Glu Leu Glu
 145 150 155 160
 Gln His Leu Glu Gln Glu Gln Glu Phe Gln Val Asn Lys Leu Met Lys
 165 170 175
 Lys Ile Lys Lys Leu Glu Asn Asp Thr Ile Ser Lys Gln Leu Thr Leu
 180 185 190
 Glu Gln Leu Arg Arg Glu Lys Ile Asp Leu Glu Asn Thr Leu Glu Gln
 195 200 205
 Glu Gln Glu Ala Leu Val Asn Arg Leu Trp Lys Arg Met Asp Lys Leu
 210 215 220
 Glu Ala Glu Thr Arg Ile Leu Gln Glu Lys Leu Asp Gln Pro Val Ser
 225 230 235 240
 Ala Pro Pro Ser Pro Arg Asp Ile Ser Met Glu Ile Asp Ser Pro Glu
 245 250 255
 Asn Met Met Arg His Ile Arg Phe Leu Lys Asn Glu Val Glu Arg Leu
 260 265 270
 Lys Lys Gln Leu Arg Ala Ala Gln Leu Gln His Ser Glu Lys Met Ala
 275 280 285
 Gln Tyr Leu Glu Glu Glu Arg His Met Arg Glu Glu Asn Leu Arg Leu
 290 295 300
 Gln Arg Lys Leu Gln Arg Glu Met Glu Arg Arg Glu Ala Leu Cys Arg
 305 310 315 320
 Gln Leu Ser Glu Ser Glu Ser Ser Leu Glu Met Asp Asp Glu Arg Tyr

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325								330				335					
Phe	Asn	Glu	Met	Ser	Ala	Gln	Gly	Leu	Arg	Pro	Arg	Thr	Val	Ser	Ser		
			340					345					350				
Pro	Ile	Pro	Tyr	Thr	Pro	Ser	Pro	Ser	Ser	Ser	Arg	Pro	Ile	Ser	Pro		
		355					360					365					
Gly	Leu	Ser	Tyr	Ala	Ser	His	Thr	Val	Gly	Phe	Thr	Pro	Pro	Thr	Ser		
	370					375					380						
Leu	Thr	Arg	Ala	Gly	Met	Ser	Tyr	Tyr	Asn	Ser	Pro	Gly	Leu	His	Val		
385					390					395					400		
Gln	His	Met	Gly	Thr	Ser	His	Gly	Ile	Thr	Arg	Pro	Ser	Pro	Arg	Arg		
				405					410					415			
Ser	Asn	Ser	Pro	Asp	Lys	Phe	Lys	Arg	Pro	Thr	Pro	Pro	Pro	Ser	Pro		
			420					425					430				
Asn	Thr	Gln	Thr	Pro	Val	Gln	Pro	Pro	Pro	Pro	Pro	Pro	Pro	Pro	Pro		
		435					440					445					
Met	Gln	Pro	Thr	Val	Pro	Ser	Gly	Ser	His	Leu	Ala	Ala	Tyr	Ser	Phe		
	450					455					460						
Ala	Thr	Phe	Gly	Ala	His	Leu	Leu	Pro	Ala	Leu	Met	His	Glu	Leu	Ser		
465					470					475					480		
Leu	Asn	Phe	Lys	Leu	Gly	Leu	Ile	Gln	Trp	Ser	Arg	Leu	Leu	Asn	Ala		
			485					490						495			
Lys	Gly	Ser	Phe	Ser	Gly	Ile	Phe	Gly	Tyr	Asp	Leu	Phe	Ala	Leu	Arg		
			500					505					510				
Leu	Ser	Arg	Leu	His	Tyr	Pro	Leu	Cys	Cys	Lys	Cys	Leu	Ser	Glu	Met		
		515					520					525					
Gln	Pro	Val	Leu	Trp	Val	Tyr	Asn	Thr	Asn	Gln	Thr	Thr	Phe	Ser	Ile		
	530					535					540						
Ser	Val	Leu	Leu	Glu	Ser	Ser	Cys	Thr	Ser	Ile	Pro	Trp	Leu	Glu	Pro		
545					550					555					560		
Ser	Leu	Phe	Gly	Ile	Trp	Tyr	Phe	Ser	Ser	Ser	Val	Gln	Phe	Leu	Leu		
				565				570						575			
Gly	Pro	Glu	Leu	His	Ser	Pro	Gly	Phe									
			580					585									

<210> 166

<211> 3011

<212> DNA

<213> Homo sapiens

<400> 166

ctgctgctcc tctctctttc ccagcccgcc gcggccatgg cggacagcgc cagcgagagc 60

127/299

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tcgacctcgg gcggcggcgg tggcggcggg ggaggcggcg gcggtgggaa gtcgggggggc 180
attgtcatct cgccgttccg cctggaggag ctcaccaacc gcctggcctc gctgcagcaa 240
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gaggagaacc gcgacctgcg caaagccagc gttaccatcc aagccagggc tgagcaggaa 360
gaagaattca ttagtaacac tttattcaag aaaattcagg ctttgcagaa ggagaaagaa 420
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actctttatt aaacacactc ctaaaaataa ggaaccatga cgattgtaga tatttaatat 3000
tgtacagtat agaaacctcc gatttttgcc ttcgaatgca gtatttaaga gttaacagaa 3011
aaaaaaaaa a

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<210> 167

<211> 808

<212> DNA

<213> Homo sapiens

<400> 167

128/299

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gcagtgtcga cactgacctt gactgtgggt tcccagggaa tgtggggcca gaccaggaca 120
gcccaggagc aggagacctg gggtgacgga tgcccagagc tggcacatca agggagggtt 180
cctggatcat ggcaggcttt ggctccctgg tcagagttca agtactgggg gccagggtgg 240
gggtctcggg aggcattccc agcagtccca agtggggccc aatgtgtgga tagaactttg 300
gtggaggggc ggggtggtagt gccagcagca ggggtgagcg gtgcgtgagg gccagtgcag 360
cccttgagga gcagtgattc cacactctga ggcggaacat ggtggcgcc tctcttgagc 420
gggtggctat gtagagaagt tgcctggac acttccactg tagtcggagg tcctgggctg 480
ggcctgggtg tcatttagtc ctggggcagg ggtcagggga gacagtagac caggaaccag 540
agagggtcga agtactgagt ccaagccatg ctgtgaccac acctgtcatg tagcagcttt 600
caggggcctg gctgtggggg cccgcccagg gcagagacag gcagggttcg ctggctcaga 660
tgacagccgg ttctctgcac attggaactt gtccatgggg cctcctttaa gggctcttgcc 720
ttcttctcc cctgtcatcc tcacactttt cccccctctt ccccccttc cctcatttcc 780
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<210> 168

<211> 271

<212> PRT

<213> Homo sapiens

<400> 168

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Met Glu Asp Ser His Lys Ser Thr Thr Ser Glu Thr Ala Pro Gln Pro
 1              5              10              15

Gly Ser Ala Val Gln Gly Ala His Ile Ser His Ile Ala Gln Gln Val
          20              25              30

Ser Ser Leu Ser Glu Ser Glu Glu Ser Gln Asp Ser Ser Asp Ser Ile
      35              40              45

Gly Ser Ser Gln Lys Ala His Gly Ile Leu Ala Arg Arg Pro Ser Tyr
 50              55              60

Arg Lys Ile Leu Lys Asp Leu Ser Ser Glu Asp Thr Arg Gly Arg Lys
 65              70              75              80

Gly Asp Gly Glu Asn Ser Gly Val Ser Ala Ala Val Thr Ser Met Ser
          85              90              95

Val Pro Thr Pro Ile Tyr Gln Thr Ser Ser Gly Gln Tyr Ile Ala Ile
      100              105              110

Ala Pro Asn Gly Ala Leu Gln Leu Ala Ser Pro Gly Thr Asp Gly Val
      115              120              125

Gln Gly Leu Gln Thr Leu Thr Met Thr Asn Ser Gly Ser Thr Gln Gln
      130              135              140

Gly Thr Thr Ile Leu Gln Tyr Ala Gln Thr Ser Asp Gly Gln Gln Ile
      145              150              155              160

Leu Val Pro Ser Asn Gln Val Val Val Gln Thr Ala Ser Gly Asp Met
          165              170              175

Gln Thr Tyr Gln Ile Arg Thr Thr Pro Ser Ala Thr Ser Leu Pro Gln
      180              185              190

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Thr Val Val Met Thr Ser Pro Val Thr Leu Thr Ser Gln Thr Thr Lys
 195 200 205

Thr Asp Asp Pro Gln Leu Lys Arg Glu Ile Arg Leu Met Lys Asn Arg
 210 215 220

Glu Ala Ala Arg Glu Cys Arg Arg Lys Lys Lys Glu Tyr Val Lys Cys
 225 230 235 240

Leu Glu Asn Arg Val Ala Val Leu Glu Asn Gln Asn Lys Thr Leu Ile
 245 250 255

Glu Glu Leu Lys Thr Leu Lys Asp Leu Tyr Ser Asn Lys Ser Val
 260 265 270

<210> 169
 <211> 816
 <212> DNA
 <213> Homo sapiens

<400> 169
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 tcccaggact catccgacag cataggctcc tcacagaaag cccacgggat cctagcacgg 180
 cgcccatctt acagaaaaat ttgaaagac ttatcttctg aagatacacg gggcagaaaa 240
 ggagacggag aaaattcttg agtttctgct gctgtcactt ctatgtctgt tccaactccc 300
 atctatcaga ctagcagcgg acagtacatt gccattgccc caaatggagc cttacagttg 360
 gcaagtccag gcacagatgg agtacaggga cttcagacat taaccatgac aaattcaggc 420
 agtactcagc aaggtacaac tattcttcag tatgcacaga cctctgatgg acagcagata 480
 cttgtgccca gcaatcaggt ggtcgtacaa actgcatcag gagatatgca aacatatcag 540
 atccgaacta caccttcagc tacttctctg ccacaaaactg tggtgatgac atctcctgtg 600
 actctcacct ctgagacaac taagacagat gacccccaat tgaaaagaga aataagggtta 660
 atgaaaaaca gagaagctgc tcgagaatgt cgcagaaaga agaaagaata tgtgaaatgc 720
 ctggaaaacc gagttgcagt cctggaaaat caaaataaaa ctctaataga agagttaaaa 780
 actttgaagg atctttattc caataaaagt gtttga 816

<210> 170
 <211> 117
 <212> PRT
 <213> Homo sapiens

<400> 170
 Thr Gly Ser Tyr Ser Gln Ala Pro Ser Gln Tyr Ser Gln Gln Ser Ser
 1 5 10 15

Ser Tyr Gly Gln Gln Ile Ala Ile Ala Pro Asn Gly Ala Leu Gln Leu
 20 25 30

Ala Ser Pro Gly Thr Asp Gly Val Gln Gly Leu Gln Thr Leu Thr Met
 35 40 45

Thr Asn Ser Gly Ser Thr Gln Gln Gly Thr Thr Ile Leu Gln Tyr Ala
 50 55 60

Gln Thr Ser Asp Gly Gln Gln Ile Leu Val Pro Ser Asn Gln Val Val
 65 70 75 80

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Val Gln Thr Ala Ser Gly Asp Met Pro Thr Tyr Gln Ile Arg Thr Thr
85 90 95

Pro Ser Ala Thr Ser Leu Pro Gln Thr Val Val Met Thr Ser Pro Val
100 105 110

Thr Leu Thr Ser Gln
115

<210> 171
<211> 353
<212> DNA
<213> Homo sapiens

<400> 171
aactggatcc tacagccaag ctccaagtca atatagccaa cagagcagca gctacgggca 60
gcagattgcc attgccccaa atggagcctt acagttggca agtccaggca cagatggagt 120
acagggactt cagacattaa ccatgacaaa ttcaggcagt actcagcaag gtacaactat 180
tcttcagtat gcacagacct ctgatggaca gcagatactt gtgccagca atcagggtgg 240
cgtacaaact gcatacaggag atatgccaac atatcagatc cgaactacac cttcagctac 300
ttctctgcca caaactgtgg tgatgacatc tcctgtgact ctcacctctc aga 353

<210> 172
<211> 500
<212> DNA
<213> Homo sapiens

<400> 172
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agagtgttac atcagggtggc caggaattac cttaggtaat tcctccactc caaaccttc 120
agtgacttcc atgacatgaa ataggaagtc attggagggt ttgagcagag gaatgacctg 180
ttttaaaagg ctactcagg ctgctgtatg gtgaatagag ttgcgaacag aggccatagg 240
ataacagggt tttgttgaga aagtggtttc attttgaggg ctaggtggaa agacctgagg 300
ttgtaaccag tagtggagag ggaaggaaaa ttaactcagg gggagtgaat ctgtagacct 360
acttgagata agatactcgc tgggttaggt aggaggggca gataggatat ctaggcttgg 420
agaggctggc aactcaaata taatggatac ttaatttttt tttttttttt tgcaggggtg 480
agcacagaca ggatcgcagg 500

<210> 173
<211> 521
<212> DNA
<213> Homo sapiens

<400> 173
cccctaaacc agatggccca ggagggggac caggtggctc tcacatgggt aagaaaggca 60
gacctggtgc tagggagctg ggaccaaaga atccttaatt tttcagcggg gaggctcggg 120
gaacataggg gaatgggaat atgatagatc ttgtttcttt tgtcctaggg ggtaactacg 180
gggatgatcg tcgtgggtggc agaggaggct atgatcgagg cggctaccgg ggccgcggcg 240
gggaccgtgg aggccttcga gggggccggg gtgggtgggga cagagggtggc tttggccctg 300
gcaagatgga ttccagacct tctgcagtca gaaagtttct gcagtaattt agagatggta 360
gtgaattgat ctgattgga aacaatggaa ttagaagtgt ttagattctt ctaagcaaag 420
gttttaaaaa ctcattttta aagaatgagt taagggccgg gcattggtggc tcacacctgt 480
aatcccagca ctttgggaga ccagagggtg gtggatcacc t 521

131/299

<210> 174

<211> 75

<212> PRT

<213> Homo sapiens

<400> 174

Tyr Ser Gln Gln Ser Ser Gln Pro Tyr Gly Gln Gln Ser Tyr Ser Gly
 1 5 10 15

Tyr Ser Gln Ser Thr Asp Thr Ser Gly Tyr Gly Gln Ser Ser Tyr Ser
 20 25 30

Ser Tyr Gly Gln Ser Gln Asn Met Phe Lys Lys Glu Val Tyr Leu His
 35 40 45

Thr Ser Pro His Leu Lys Ala Asp Val Leu Phe Gln Thr Asp Pro Thr
 50 55 60

Ala Glu Met Ala Ala Glu Ser Leu Pro Phe Ser
 65 70 75

<210> 175

<211> 225

<212> DNA

<213> Homo sapiens

<400> 175

tattcccagc agagcagtcg gccctacgga cagcagaggtt acagtgggta tagccagtc 60
 acggacactt caggctatgg ccagagcagc tattcttctt atggccagag ccagaacatg 120
 ttcaagaagg aagtgtatct tcatacatca ccacacctga aagcagatgt gcttttccag 180
 actgatccaa ctgcagagat ggcagctgag tcattgcctt tctcc 225

<210> 176

<211> 78

<212> PRT

<213> Homo sapiens

<400> 176

Gly Asp Trp Lys Cys Pro Asn Pro Thr Cys Glu Asn Met Asn Phe Ser
 1 5 10 15

Trp Arg Asn Glu Cys Asn Gln Cys Lys Ala Pro Lys Pro Asp Gly Pro
 20 25 30

Gly Gly Gly Pro Gly Gly Ser His Met Gly Val Phe Lys Lys Glu Val
 35 40 45

Tyr Leu His Thr Ser Pro His Leu Lys Ala Asp Val Leu Phe Gln Thr
 50 55 60

Asp Pro Thr Ala Glu Met Ala Ala Glu Ser Leu Pro Phe Ser
 65 70 75

<210> 177

132/299

<211> 235

<212> DNA

<213> Homo sapiens

<400> 177

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tggtgactgg aagtgtccta atcccacctg tgagaatatg aacttctctt ggaggaatga 60
atgcaaccag tgtaaggccc ctaaaccaga tggcccagga gggggaccag gtggctctca 120
catgggggtg ttcaagaagg aagtgtatct tcatacatca ccacacctga aagcagatgt 180
gcttttccag actgatccaa ctgcagagat ggcagctgag tcattgcctt tctcc 235

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<210> 178

<211> 526

<212> PRT

<213> Homo sapiens

<400> 178

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Met Ala Ser Asn Asp Tyr Thr Gln Gln Ala Thr Gln Ser Tyr Gly Ala
  1             5             10             15

Tyr Pro Thr Gln Pro Gly Gln Gly Tyr Ser Gln Gln Ser Ser Gln Pro
          20             25             30

Tyr Gly Gln Gln Ser Tyr Ser Gly Tyr Ser Gln Ser Thr Asp Thr Ser
          35             40             45

Gly Tyr Gly Gln Ser Ser Tyr Ser Ser Tyr Gly Gln Ser Gln Asn Thr
          50             55             60

Gly Tyr Gly Thr Gln Ser Thr Pro Gln Gly Tyr Gly Ser Thr Gly Gly
          65             70             75             80

Tyr Gly Ser Ser Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser
          85             90             95

Tyr Pro Gly Tyr Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser
          100            105            110

Tyr Gly Ser Ser Ser Gln Ser Ser Ser Tyr Gly Gln Pro Gln Ser Gly
          115            120            125

Ser Tyr Ser Gln Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly
          130            135            140

Gln Gln Gln Ser Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln
          145            150            155            160

Tyr Asn Ser Ser Ser Gly Gly Gly Gly Gly Gly Gly Gly Gly Asn
          165            170            175

Tyr Gly Gln Asp Gln Ser Ser Met Ser Ser Gly Gly Gly Ser Gly Gly
          180            185            190

Gly Tyr Gly Asn Gln Asp Gln Ser Gly Gly Gly Gly Ser Gly Gly Tyr
          195            200            205

Gly Gln Gln Asp Arg Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly Gly
          210            215            220

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Gly Gly Gly Gly Gly Gly Gly Tyr Asn Arg Ser Ser Gly Gly Tyr Glu
 225 230 235 240
 Pro Arg Gly Arg Gly Gly Gly Arg Gly Gly Arg Gly Gly Met Gly Gly
 245 250 255
 Ser Asp Arg Gly Gly Phe Asn Lys Phe Gly Gly Pro Arg Asp Gln Gly
 260 265 270
 Ser Arg His Asp Ser Glu Gln Asp Asn Ser Asp Asn Asn Thr Ile Phe
 275 280 285
 Val Gln Gly Leu Gly Glu Asn Val Thr Ile Glu Ser Val Ala Asp Tyr
 290 295 300
 Phe Lys Gln Ile Gly Ile Ile Lys Thr Asn Lys Lys Thr Gly Gln Pro
 305 310 315 320
 Met Ile Asn Leu Tyr Thr Asp Arg Glu Thr Gly Lys Leu Lys Gly Glu
 325 330 335
 Ala Thr Val Ser Phe Asp Asp Pro Pro Ser Ala Lys Ala Ala Ile Asp
 340 345 350
 Trp Phe Asp Gly Lys Glu Phe Ser Gly Asn Pro Ile Lys Val Ser Phe
 355 360 365
 Ala Thr Arg Arg Ala Asp Phe Asn Arg Gly Gly Gly Asn Gly Arg Gly
 370 375 380
 Gly Arg Gly Arg Gly Gly Pro Met Gly Arg Gly Gly Tyr Gly Gly Gly
 385 390 395 400
 Gly Ser Gly Gly Gly Gly Arg Gly Gly Phe Pro Ser Gly Gly Gly Gly
 405 410 415
 Gly Gly Gly Gln Gln Arg Ala Gly Asp Trp Lys Cys Pro Asn Pro Thr
 420 425 430
 Cys Glu Asn Met Asn Phe Ser Trp Arg Asn Glu Cys Asn Gln Cys Lys
 435 440 445
 Ala Pro Lys Pro Asp Gly Pro Gly Gly Gly Pro Gly Gly Ser His Met
 450 455 460
 Gly Gly Asn Tyr Gly Asp Asp Arg Arg Gly Gly Arg Gly Gly Tyr Asp
 465 470 475 480
 Arg Gly Gly Tyr Arg Gly Arg Gly Gly Asp Arg Gly Gly Phe Arg Gly
 485 490 495
 Gly Arg Gly Gly Gly Asp Arg Gly Gly Phe Gly Pro Gly Lys Met Asp
 500 505 510
 Ser Arg Gly Glu His Arg Gln Asp Arg Arg Glu Arg Pro Tyr
 515 520 525

134/299

<210> 179
 <211> 1824
 <212> DNA
 <213> Homo sapiens

<400> 179
 atgctcagtc ctccaggcgt cgggtgctcag cgggtgttggg acttcggttgc ttgcttgcct 60
 gtgcgcgcgt gcgcggacat ggctctaaac gattataccc aacaagcaac ccaaagctat 120
 ggggcctacc ccaccagcc cgggcagggc tattcccagc agagcagtca gccctacgga 180
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 agcagttctc agagcagcag ctatgggcag cccagagtg ggagctacag ccagcagcct 480
 agctatggtg gacagcagca aagctatgga cagcagcaaa gctataatcc ccctcagggc 540
 tatggacagc agaaccagta caacagcagc agtggtggtg gaggtggagg tggaggtgga 600
 ggtaactatg gccaaagatca atcctccatg agtagtggtg gtggcagtggt tggcgggttat 660
 ggcaatcaag accagagtggt tggaggtggc agcgggtggct atggacagca ggaccgtgga 720
 ggccgcggca ggggtggcag tgggtggcggc ggccggcggc gcgggtggtg ttacaaccgc 780
 agcagtgggt gctatgaacc cagaggtcgt ggaggtggcc gtggaggcag aggtggcatg 840
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 catgactccg aacaggataa ttcagacaac aacaccatct ttgtgcaagg cctgggtgag 960
 aatgttacia ttgagtctgt ggctgattac ttcaagcaga ttggtattat taagacaaac 1020
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 ggtggcgggt gaggacagca gcgagctggt gactggaagt gtcctaatac cactgtgag 1380
 aatatgaact tctcttggag gaatgaatgc aaccagtgtg agggccctaa accagatggc 1440
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 cgagggggcc ggggtggtgg ggacagaggt ggctttggcc ctggcaagat ggattccagg 1620
 ggtgagcaca gacaggatcg caggagagg ccgtattaat tagcctggct cccaggttc 1680
 tggaaacagt ttttgtcctg taccagtggt taccctcgtt attttgtaac cttccaattc 1740
 ctgatcacc aagggttttt tttgtgtcgg actatgtaat tgtaactata cctctgggtc 1800
 ccattaaaag tgaccatttt agtt 1824

<210> 180
 <211> 195
 <212> PRT
 <213> Homo sapiens

<400> 180
 Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser Tyr Pro Gly Tyr
 1 5 10 15
 Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser Tyr Gly Ser Ser
 20 25 30
 Ser Gln Ser Ser Ser Tyr Gly Gln Pro Gln Ser Gly Ser Tyr Ser Gln
 35 40 45
 Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly Gln Gln Gln Ser
 50 55 60

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Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln Tyr Asn Ser Ser
 65 70 75 80
 Ser Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Asn Tyr Gly Gln Asp
 85 90 95
 Gln Ser Ser Met Ser Ser Gly Gly Gly Ser Gly Gly Gly Tyr Gly Asn
 100 105 110
 Gln Asp Gln Ser Gly Gly Gly Gly Ser Gly Gly Tyr Gly Gln Gln Asp
 115 120 125
 Arg Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly Gly Gly Ala Ala Ala
 130 135 140
 Val Val Val Thr Thr Ala Ala Val Val Ala Met Asn Pro Glu Val Val
 145 150 155 160
 Glu Val Ala Val Glu Ala Glu Val Ala Trp Ala Glu Val Thr Val Val
 165 170 175
 Ala Ser Ile Asn Leu Val Cys Ser Arg Arg Lys Cys Ile Phe Ile His
 180 185 190
 His His Ser
 195

<210> 181

<211> 652

<212> DNA

<213> Homo sapiens

<400> 181

cagagctccc aatcgtctta cgggcagcag tcctcctacc ctggctatgg ccagcagcca 60
 gctcccagca gcacctcggg aagttacggg agcagttctc agagcagcag ctatgggcag 120
 ccccagagtg ggagctacag ccagcagcct agctatgggtg gacagcagca aagctatgga 180
 cagcagcaaaa gctataatcc ccctcagggc tatggacagc agaaccagta caacagcagc 240
 agtgggtgggtg gaggtggagg tggaggtgga ggtaactatg gccaagatca atcctccatg 300
 agtagtggtg gtggcagtgg tggcggttat ggcaatcaag accagagtgg tggaggtggc 360
 agcgggtggct atggacagca ggaccgtgga ggccgcggca ggggtggcag tgggtggcggc 420
 ggggcggcgg cggtgggtgt tacaaccgca gcagtgggtg ctatgaaccc agaggtcgtg 480
 gaggtggccg tggaggcaga ggtggcatgg gcggaagtga ccgtgggtggc ttcaataaat 540
 ttggtgtgtt caagaaggaa gtgtatcttc atacatcacc actcctgaaa gcagatgtgc 600
 ttttcagac tgatccaact gcagagatgg cagctgagtc attgcctttc tc 652

<210> 182

<211> 462

<212> PRT

<213> Homo sapiens

<400> 182

Met Ala Ser Asn Asp Tyr Thr Gln Gln Ala Thr Gln Ser Tyr Gly Ala
 1 5 10 15
 Tyr Pro Thr Gln Pro Gly Gln Gly Tyr Ser Gln Gln Ser Ser Gln Pro
 20 25 30

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Tyr Gly Gln Gln Ser Tyr Ser Gly Tyr Ser Gln Ser Thr Asp Thr Ser
 35 40 45
 Gly Tyr Gly Gln Ser Ser Tyr Ser Ser Tyr Gly Gln Ser Gln Asn Thr
 50 55 60
 Gly Tyr Gly Thr Gln Ser Ser Thr Pro Gln Gly Tyr Gly Ser Thr Gly Gly
 65 70 75 80
 Tyr Gly Ser Ser Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser
 85 90 95
 Tyr Pro Gly Tyr Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser
 100 105 110
 Tyr Gly Ser Ser Ser Gln Ser Ser Tyr Gly Gln Pro Gln Ser Gly
 115 120 125
 Ser Tyr Ser Gln Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly
 130 135 140
 Gln Gln Gln Ser Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln
 145 150 155 160
 Tyr Asn Ser Ser Ser Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Asn
 165 170 175
 Tyr Gly Gln Asp Gln Ser Ser Met Ser Ser Gly Gly Gly Ser Gly Gly
 180 185 190
 Gly Tyr Gly Asn Gln Asp Gln Ser Gly Gly Gly Gly Ser Gly Gly Tyr
 195 200 205
 Gly Gln Gln Asp Arg Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly Gly
 210 215 220
 Gly Gly Gly Gly Gly Gly Gly Tyr Asn Arg Ser Ser Gly Gly Tyr Glu
 225 230 235 240
 Pro Arg Gly Arg Gly Gly Gly Arg Gly Gly Arg Gly Gly Met Gly Gly
 245 250 255
 Ser Asp Arg Gly Gly Phe Asn Lys Phe Gly Val Phe Lys Lys Glu Val
 260 265 270
 Tyr Leu His Thr Ser Pro His Leu Lys Ala Asp Val Leu Phe Gln Thr
 275 280 285
 Asp Pro Thr Ala Glu Met Ala Ala Glu Ser Leu Pro Phe Ser Phe Gly
 290 295 300
 Thr Leu Ser Ser Trp Glu Leu Glu Ala Trp Tyr Glu Asp Leu Gln Glu
 305 310 315 320
 Val Leu Ser Ser Asp Glu Asn Gly Gly Thr Tyr Val Ser Pro Pro Gly
 325 330 335

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Asn Glu Glu Glu Glu Ser Lys Ile Phe Thr Thr Leu Asp Pro Ala Ser
 340 345 350
 Leu Ala Trp Leu Thr Glu Glu Glu Pro Glu Pro Ala Glu Val Thr Ser
 355 360 365
 Thr Ser Gln Ser Pro His Ser Pro Asp Ser Ser Gln Ser Ser Leu Ala
 370 375 380
 Gln Glu Glu Glu Glu Glu Asp Gln Gly Arg Thr Arg Lys Arg Lys Gln
 385 390 395 400
 Ser Gly His Ser Pro Ala Arg Ala Gly Lys Gln Arg Met Lys Glu Lys
 405 410 415
 Glu Gln Glu Asn Glu Arg Lys Val Ala Gln Leu Ala Glu Glu Asn Glu
 420 425 430
 Arg Leu Lys Gln Glu Ile Glu Arg Leu Thr Arg Glu Val Glu Ala Thr
 435 440 445
 Arg Arg Ala Leu Ile Asp Arg Met Val Asn Leu His Gln Ala
 450 455 460

<210> 183

<211> 1678

<212> DNA

<213> Homo sapiens

<400> 183

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gcggccgctg tcggtgctca gcggtgttgg aacttcgttg cttgcttgcc tgtgcgcgcg 60
tgccgcggaca tggcctcaaa cgattatacc caacaagcaa cccaaagcta tggggcctac 120
cccaccagc ccgggcaggg ctattcccag cagagcagtc agccctacgg acagcagagt 180
tacagtgggt atagccagtc cacggacact tcaggctatg gccagagcag ctattcttct 240
tatggccaga gccagaacac aggctatgga actcagtcaa ctcccagggt atatggctcg 300
actggcggct atggcagtag ccagagctcc caatcgtctt acgggcagca gtcctcctac 360
cttggtctat gccagcagcc agctcccagc agcacctcgg gaagttacgg tagcagttct 420
cagagcagca gctatgggca gcccagagt gggagctaca gccagcagcc tagctatggt 480
ggacagcagc aaagctatgg acagcagcaa agctataatc cccctcagggt ctatggacag 540
cagaaccagt acaacagcag cagtgggtgg ggaggtggag gtggaggtgg aggtaactat 600
ggccaagatc aatcctccat gtagtagtgt ggtggcagtg gtggcggtta tggcaatcaa 660
gaccagagtg gtggaggtgg cagcgggtggc tatggacagc aggaccgtgg aggccgcggc 720
aggggtggca gtggtggcgg cggcggcggc ggcggtgttg gttacaaccg cagcagtggt 780
ggctatgaac ccagaggtcg tggaggtggc cgtggaggca gaggtggcat gggcggaagt 840
gaccgtggtg gcttcaataa atttggtgtg ttcaagaagg aagtgtatct tcatacatca 900
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ctgcaagagg tcctgtcttc agatgaaaat gggggtacct atgtttcacc tcctggaaat 1080
gaagaggaag aatcaaaaat cttcaccact cttgacctg cttctctggc ttggctgact 1140
gaggaggagc cagaaccagc agaggtcaca agcacctccc agagccctca ctctccagat 1200
tccagtcaga gtcctctggc tcaggaggaa gaggaggaag accaaggag aaccaggaaa 1260
cggaacacaga gtggtcattc cccagcccgg gctggaaagc agcgcatgaa ggagaaagaa 1320
caggagaatg aaaggaaagt ggcacagcta gctgaagaga atgaacggct caagcaggaa 1380
atcgagcgcc tgaccaggga agtagaggcg actcgccgag ctctgattga ccgaatggtg 1440
aatctgcacc aagcatgaac aattgggagc atcagctccc cacttgggpc acactacca 1500
cctttcccag aagtggctac tgactaccct ctcactatgt ccaatgatgt gacctcaat 1560
cccacatacg caggggggag gcttggagta gacaaaagga aaggtctcag cttgtatata 1620

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gagattgtac atttatttat tactgtccct atctattaaa gtgactttct atgaaaaa 1678

<210> 184

<211> 525

<212> PRT

<213> Homo sapiens

<400> 184

Met Ala Ser Asn Asp Tyr Thr Gln Gln Ala Thr Gln Ser Tyr Gly Ala
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Tyr Pro Thr Gln Pro Gly Gln Gly Tyr Ser Gln Gln Ser Ser Gln Pro
 20 25 30

Tyr Gly Gln Gln Ser Tyr Ser Gly Tyr Ser Gln Ser Thr Asp Thr Ser
 35 40 45

Gly Tyr Gly Gln Ser Ser Tyr Ser Ser Tyr Gly Gln Ser Gln Asn Ser
 50 55 60

Tyr Gly Thr Gln Ser Thr Pro Gln Gly Tyr Gly Ser Thr Gly Gly Tyr
 65 70 75 80

Gly Ser Ser Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser Tyr
 85 90 95

Pro Gly Tyr Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser Tyr
 100 105 110

Gly Ser Ser Ser Gln Ser Ser Ser Tyr Gly Gln Pro Gln Ser Gly Ser
 115 120 125

Tyr Ser Gln Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly Gln
 130 135 140

Gln Gln Ser Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln Tyr
 145 150 155 160

Asn Ser Ser Ser Gly Gly Gly Gly Gly Gly Gly Gly Gly Asn Tyr
 165 170 175

Gly Gln Asp Gln Ser Ser Met Ser Ser Gly Gly Gly Ser Gly Gly Gly
 180 185 190

Tyr Gly Asn Gln Asp Gln Ser Gly Gly Gly Gly Ser Gly Gly Tyr Gly
 195 200 205

Gln Gln Asp Arg Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly Gly Gly
 210 215 220

Gly Gly Gly Gly Gly Gly Tyr Asn Arg Ser Ser Gly Gly Tyr Glu Pro
 225 230 235 240

Arg Gly Arg Gly Gly Gly Arg Gly Gly Arg Gly Gly Met Gly Gly Ser
 245 250 255

Asp Arg Gly Gly Phe Asn Lys Phe Gly Gly Pro Arg Asp Gln Gly Ser

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260										265					270				
Arg	His	Asp	Ser	Glu	Gln	Asp	Asn	Ser	Asp	Asn	Asn	Thr	Ile	Phe	Val				
		275						280					285						
Gln	Gly	Leu	Gly	Glu	Asn	Val	Thr	Ile	Glu	Ser	Val	Ala	Asp	Tyr	Phe				
	290					295					300								
Lys	Gln	Ile	Gly	Ile	Ile	Lys	Thr	Asn	Lys	Lys	Thr	Gly	Gln	Pro	Met				
305					310					315					320				
Ile	Asn	Leu	Tyr	Thr	Asp	Arg	Glu	Thr	Gly	Lys	Leu	Lys	Gly	Glu	Ala				
				325					330					335					
Thr	Val	Ser	Phe	Asp	Asp	Pro	Pro	Ser	Ala	Lys	Ala	Ala	Ile	Asp	Trp				
			340					345					350						
Phe	Asp	Gly	Lys	Glu	Phe	Ser	Gly	Asn	Pro	Ile	Lys	Val	Ser	Phe	Ala				
		355					360					365							
Thr	Arg	Arg	Ala	Asp	Phe	Asn	Arg	Gly	Gly	Gly	Asn	Gly	Arg	Gly	Gly				
	370					375					380								
Arg	Gly	Arg	Gly	Gly	Pro	Met	Gly	Arg	Gly	Gly	Tyr	Gly	Gly	Gly	Gly				
385					390					395					400				
Ser	Gly	Gly	Gly	Gly	Arg	Gly	Gly	Phe	Pro	Ser	Gly	Gly	Gly	Gly	Gly				
				405				410						415					
Gly	Gly	Gln	Gln	Arg	Ala	Gly	Asp	Trp	Lys	Cys	Pro	Asn	Pro	Thr	Cys				
		420					425						430						
Glu	Asn	Met	Asn	Phe	Ser	Trp	Arg	Asn	Glu	Cys	Asn	Gln	Cys	Lys	Ala				
	435						440					445							
Pro	Lys	Pro	Asp	Gly	Pro	Gly	Gly	Gly	Pro	Gly	Gly	Ser	His	Met	Gly				
	450					455					460								
Gly	Asn	Tyr	Gly	Asp	Asp	Arg	Arg	Gly	Gly	Arg	Gly	Gly	Tyr	Asp	Arg				
465					470					475					480				
Gly	Gly	Tyr	Arg	Gly	Arg	Gly	Gly	Asp	Arg	Gly	Gly	Phe	Arg	Gly	Gly				
			485					490						495					
Arg	Gly	Gly	Gly	Asp	Arg	Gly	Gly	Phe	Gly	Pro	Gly	Lys	Met	Asp	Ser				
			500				505						510						
Arg	Gly	Glu	His	Arg	Gln	Asp	Arg	Arg	Glu	Arg	Pro	Tyr							
	515					520						525							

<210> 185

<211> 1822

<212> DNA

<213> Homo sapiens

<400> 185

gcggccgctg gcgtcggtgc tcagcgggtg tggaacttcg ttgcttgctt gcctgtgcgc 60

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gcgtgcgcgg acatggcctc aaacgattat acccaacaag caacccaaag ctatggggcc 120
taccaccacc agcccgggca gggctattcc cagcagagca gtcagcccta cggacagcag 180
agttacagtg gttatagcca gtccacggac acttcaggct atggccagag cagctattct 240
tcttatggcc agagccagaa cagctatgga actcagtcaa ctcccagggt atatggctcg 300
actggcggct atggcagtag ccagagctcc caatcgtctt acgggcagca gtcctcctat 360
cctggctatg gccagcagcc agctcccagc agcacctcgg gaagttacgg tagcagttct 420
cagagcagca gctatgggca gccccagagt gggagctaca gccagcagcc tagctatggg 480
ggacagcagc aaagctatgg acagcagcaa agctataatc cccctcagggt ctatggacag 540
cagaaccagt acaacagcag cagtgggtgg ggaggtggag gtggaggtgg aggtaactat 600
ggccaagatc aatcctccat gagtagtggt ggtggcagtg gtggcgggta tggcaatcaa 660
gaccagagtg gtggaggtgg cagcgggtgg tatggacagc aggaccgtgg aggcgcgggc 720
aggggtggca gtgggtggcg cggcggcgcc ggcggtgggt gttacaaccg cagcagtggt 780
ggctatgaac ccagaggtcg tggaggtggc cgtggaggca gaggtggcat gggcgggaag 840
gaccgtgggt gcttcaataa atttgggtgg cctcgggacc aaggatcacg tcatgactcc 900
gaacaggata attcagacaa caacaccatc tttgtgcaag gcctgggtga gaatgttaca 960
attgagtctg tggctgatta cttcaagcag attggtatta ttaagacaaa caagaaaacg 1020
ggacagccca tgattaatct gtacacagac agggaaactg gcaagctgaa gggagaggca 1080
acggtctctt ttgatgacct accttcagct aaagcagcta ttgactgggt tgatggtaaa 1140
gaattctccg gaaatcctat caaggtctca tttgctactc gccgggcaga ctttaatcgg 1200
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ggaggacagc agcgagctgg tgactggaag tgcctaatac ccacctgtga gaatatgaac 1380
ttctcttggg ggaatgaatg caaccagtg aaggcccta aaccagatgg ccaggagggt 1440
ggaccaggtg gctctcacat ggggggtaac tacgggggat atcgtcgtgg tggcagagga 1500
ggctatgatc gaggcggcta ccggggccgc ggcggggacc gtggaggctt ccgagggggc 1560
cgggggtggt gggacagagg tggctttggc cctggcaaga tggattccag ggggtgagcac 1620
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tttttgcct gtaccagtg ttaccctcgt tattttgtaa cttccaatt cctgatcacc 1740
caagggtttt tttgtgtcgg actatgtaat tgtaactata cctctggttc ccattaaaag 1800
tgaccatttt agttaaaaa aa 1822

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<210> 186

<211> 120

<212> DNA

<213> Homo sapiens

<400> 186

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tggtttctaa agatgaaatt aagaattggt ccacaagggt taagtgtctg gtggtaaagt 60
tgggctcgga ggcctacagt aacccaaata taagtgccac ggagaaagct aaagcagaga 120

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<210> 187

<211> 118

<212> DNA

<213> Homo sapiens

<400> 187

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tgagtgtgtg ggagacaact ccgaatgttt aattctggaa gagggatgta acattgccct 60
gaggattcga gatggtagtg aattgatcta gattggaaac aatggaatta gaagtgtt 118

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<210> 188

<211> 120

<212> DNA

<213> Homo sapiens

<400> 188

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gtgtgggaga caactccgaa tgtttaattc tggaagaggg atgtaacatt gccctgagga 60
 tgggtggctca cacctgtaat cccagcactt tgggagacca gaggtgggtg gatcaccctg 120

<210> 189
 <211> 126
 <212> PRT
 <213> Homo sapiens

<400> 189
 Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser Tyr Pro Gly Tyr
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 Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser Tyr Gly Ser Ser
 20 25 30
 Ser Gln Ser Ser Ser Tyr Gly Gln Pro Gln Ser Gly Ser Tyr Ser Gln
 35 40 45
 Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly Gln Gln Gln Ser
 50 55 60
 Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln Tyr Asn Ser Ser
 65 70 75 80
 Ser Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Val Phe Lys Lys Glu Val
 85 90 95
 Tyr Leu His Thr Ser Pro Leu Leu Lys Ala Asp Val Leu Phe Gln Thr
 100 105 110
 Asp Pro Thr Ala Glu Met Ala Ala Glu Ser Leu Pro Phe Ser
 115 120 125

<210> 190
 <211> 377
 <212> DNA
 <213> Homo sapiens

<400> 190
 cagagctccc aatcgtctta cgggcagcag tcctcctacc ctggctatgg ccagcagcca 60
 gctcccagca gcacctcggg aagttacggt agcagttctc agagcagcag ctatggggcag 120
 ccccagagtg ggagctacag ccagcagcct agctatggtg gacagcagca aagctatgga 180
 cagcagcaaa gctataatcc ccctcagggc tatggacagc agaaccagta caacagcagc 240
 agtgggtgggtg gaggtggagg tggaggtgga gtgttcaaga aggaagtgta tcttcataca 300
 tcaccactcc tgaaagcaga tgtgcttttc cagactgata caactgcaga gatggcagct 360
 gagtcattgc ctttctc 377

<210> 191
 <211> 689
 <212> PRT
 <213> Homo sapiens

<400> 191
 Pro Ser Val Ser Ser Ile Ser Arg Ile Leu Arg Ser Lys Phe Gly Lys
 1 5 10 15

Gly	Glu	Glu	Glu	Glu	Ala	Asp	Leu	Glu	Arg	Lys	Glu	Ala	Glu	Glu	Ser	
			20				25						30			
Glu	Lys	Lys	Ala	Lys	His	Ser	Ile	Asp	Gly	Ile	Leu	Ser	Glu	Arg	Ala	
			35				40						45			
Ser	Ala	Pro	Gln	Ser	Asp	Glu	Gly	Ser	Asp	Ile	Asp	Ser	Glu	Pro	Asp	
			50				55						60			
Leu	Pro	Leu	Lys	Arg	Lys	Gln	Arg	Arg	Ser	Arg	Thr	Thr	Phe	Thr	Ala	
			65				70						75			
Glu	Gln	Leu	Glu	Glu	Leu	Glu	His	Val	Ala	Phe	Glu	Arg	Thr	His	Tyr	
			85						90						95	
Pro	Asp	Ile	Tyr	Thr	Arg	Glu	Glu	Leu	Ala	Gln	Arg	Ala	Lys	Leu	Thr	
			100			105						110				
Glu	Ala	Arg	Val	Gln	Val	Trp	Phe	Ser	Asn	Arg	Arg	Ala	Arg	Trp	Arg	
			115			120						125				
Lys	Gln	Ala	Gly	Ala	Asn	Gln	Leu	Met	Ala	Phe	Asn	His	Leu	Ile	Pro	
			130			135						140				
Gly	Gly	Phe	Pro	Pro	Thr	Ala	Met	Pro	Thr	Leu	Pro	Thr	Tyr	Gln	Leu	
			145			150						155			160	
Ser	Glu	His	Ser	Tyr	Gln	Pro	Thr	Ser	Ile	Pro	Gln	Ala	Val	Ser	Asp	
			165			170						175				
Pro	Ser	Ser	Thr	Val	His	Arg	Pro	Gln	Pro	Leu	Pro	Pro	Ser	Thr	Val	
			180			185						190				
His	Gln	Ser	Thr	Ile	Pro	Ser	Asn	Pro	Asp	Ser	Ser	Ser	Ala	Tyr	Cys	
			195			200						205				
Leu	Pro	Ser	Thr	Arg	His	Gly	Phe	Ser	Ser	Tyr	Thr	Asp	Ser	Phe	Val	
			210			215						220				
Pro	Pro	Ser	Gly	Pro	Ser	Asn	Pro	Met	Asn	Pro	Thr	Ile	Gly	Asn	Gly	
			225			230						235			240	
Leu	Ser	Pro	Gln	Asn	Ser	Ile	Arg	His	Asn	Leu	Ser	Leu	His	Ser	Lys	
			245			250						255				
Phe	Ile	Arg	Val	Gln	Asn	Glu	Gly	Thr	Gly	Lys	Ser	Ser	Trp	Trp	Met	
			260			265						270				
Leu	Asn	Pro	Glu	Gly	Gly	Lys	Ser	Gly	Lys	Ser	Pro	Arg	Arg	Arg	Ala	
			275			280						285				
Ala	Ser	Met	Asp	Asn	Asn	Ser	Lys	Phe	Ala	Lys	Ser	Arg	Ser	Arg	Ala	
			290			295						300				
Ala	Lys	Lys	Lys	Ala	Ser	Leu	Gln	Ser	Gly	Gln	Glu	Gly	Ala	Gly	Asp	
			305			310						315			320	

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Ser Pro Gly Ser Gln Phe Ser Lys Trp Pro Ala Ser Pro Gly Ser His
 325 330 335
 Ser Asn Asp Asp Phe Asp Asn Trp Ser Thr Phe Arg Pro Arg Thr Ser
 340 345 350
 Ser Asn Ala Ser Thr Ile Ser Gly Arg Leu Ser Pro Ile Met Thr Glu
 355 360 365
 Gln Asp Asp Leu Gly Glu Gly Asp Val His Ser Met Val Tyr Pro Pro
 370 375 380
 Ser Ala Ala Lys Met Ala Ser Thr Leu Pro Ser Leu Ser Glu Ile Ser
 385 390 395 400
 Asn Pro Glu Asn Met Glu Asn Leu Leu Asp Asn Leu Asn Leu Leu Ser
 405 410 415
 Ser Pro Thr Ser Leu Thr Val Ser Thr Gln Ser Ser Pro Gly Thr Met
 420 425 430
 Met Gln Gln Thr Pro Cys Tyr Ser Phe Ala Pro Pro Asn Thr Ser Leu
 435 440 445
 Asn Ser Pro Ser Pro Asn Tyr Gln Lys Tyr Thr Tyr Gly Gln Ser Ser
 450 455 460
 Met Ser Pro Leu Pro Gln Met Pro Ile Gln Thr Leu Gln Asp Asn Lys
 465 470 475 480
 Ser Ser Tyr Gly Gly Met Ser Gln Tyr Asn Cys Ala Pro Gly Leu Leu
 485 490 495
 Lys Glu Leu Leu Thr Ser Asp Ser Pro Pro His Asn Asp Ile Met Thr
 500 505 510
 Pro Val Asp Pro Gly Val Ala Gln Pro Asn Ser Arg Val Leu Gly Gln
 515 520 525
 Asn Val Met Met Gly Pro Asn Ser Val Met Ser Thr Tyr Gly Ser Gln
 530 535 540
 Ala Ser His Asn Lys Met Met Asn Pro Ser Ser His Thr His Pro Gly
 545 550 555 560
 His Ala Gln Gln Thr Ser Ala Val Asn Gly Arg Pro Leu Pro His Thr
 565 570 575
 Val Ser Thr Met Pro His Thr Ser Gly Met Asn Arg Leu Thr Gln Val
 580 585 590
 Lys Thr Pro Val Gln Val Pro Leu Pro His Pro Met Gln Met Ser Ala
 595 600 605
 Leu Gly Gly Tyr Ser Ser Val Ser Ser Cys Asn Gly Tyr Gly Arg Met
 610 615 620
 Gly Leu Leu His Gln Glu Lys Leu Pro Ser Asp Leu Asp Gly Met Phe

625	630							635					640			
Ile	Glu	Arg	Leu	Asp	Cys	Asp	Met	Glu	Ser	Ile	Ile	Arg	Asn	Asp	Leu	
				645					650					655		
Met	Asp	Gly	Asp	Thr	Leu	Asp	Phe	Asn	Phe	Asp	Asn	Val	Leu	Pro	Asn	
			660					665					670			
Gln	Ser	Phe	Pro	His	Ser	Val	Lys	Thr	Thr	Thr	His	Ser	Trp	Val	Ser	
		675					680					685				

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<210> 192
<211> 3517
<212> DNA
<213> Homo sapiens
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<400> 192						
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gacggcatcc	tgagcgagcg	agcctcagca	ccccaatcag	atgaaggctc	tgatattgac	180
tctgaaccag	atttaccact	aaagaggaaa	cagcgagaaa	gccgaaccac	cttcacagca	240
gaacagctgg	aggaacttgg	gcacgttgct	tttgagagaa	ctcattacc	tgacatttat	300
actaggggag	aactggccca	gagggcgag	ctcaccgag	cccgagtaca	ggctctggttt	360
agcaaccgcc	gtgcaagatg	gaggaagcaa	gctggggcca	atcaactgat	ggctttcaac	420
catctcattc	ccgggggatt	ccctcccact	gccatgccga	ccttgccaac	gtaccagctg	480
tcggagcact	cttaccagcc	cacatctatt	ccacaagctg	tgctcagatcc	cagcagcacc	540
gttcacagac	ctcaaccgct	tcctccaagc	actgtacacc	aaagcacgat	tccttccaac	600
ccagacagca	gctctgccta	ctgcctcccc	agcaccaggc	atggattttc	cagctataca	660
gacagctttg	tgcctccgct	ggggccctac	aacccccatg	acccccaccat	tggcaattggc	720
ctctcacctc	agaattcaat	tcgtcctaac	ctgtccctac	acagcaagtt	cattcgtgtg	780
cagaatgaag	gaactggaaa	aagttcttgg	tggatgctca	atccagagg	tggcaagagc	840
gggaaatctc	ctaggagaag	agctgcattc	atggacaaca	acagtaaat	tgctaagagc	900
cgaagccgag	ctgccaagaa	gaaagcatct	ctccagttctg	gccaggaggg	tgctggggac	960
agccctggat	cacagttttc	caaattggct	gcaagccctg	gctctcacag	caatgatgac	1020
tttgataact	ggagtacatt	tcgcccctga	actagctcaa	atgctagtac	tattagtggg	1080
agactctcac	ccattatgac	cgaacaggat	gatcttggag	aaggggatgt	gcattctatg	1140
gtgtaccggc	catctgccc	aaagattggc	tctactttac	ccagttctgc	tgagataagc	1200
aatccgaaa	acatggaaaa	tcctttggat	aattctcaac	ttctctcatt	accaatacca	1260
ttactgttt	cgaccagtc	ctcaactggc	acatgatgc	agcagcgc	tggtactctg	1320
tttgcgccac	caaacaccag	tttgaattca	cccagcccaa	actacccaaa	atatacatat	1380
ggccaatcca	gcatgagccc	tttgccccag	atgcttatac	aaacacttca	ggacaataag	1440
tcgagttatg	gaggtatgag	tcagtataac	tgtgcgcctg	gactcttgaa	ggagttgctg	1500
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cccaacagcc	gggttctggg	ccagaacgtc	atgatgggccc	ctaattcggg	catgtcaacc	1620
tatggcagcc	aggcattctca	taacaaaaatg	atgaattccca	gctcccatac	ccaccctgga	1680
catgctcagc	agacatctgc	agtcaacggg	cgtcccctgc	ccacacggg	aagcaccatg	1740
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<213> Homo sapiens

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Val Glu Arg Pro Gln Met Thr Phe Gly Arg Leu Gln Gly Ile Ser Pro
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Lys Ile Met Pro Lys Lys Pro
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<213> Homo sapiens

146/299

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Ser Lys Glu Glu Trp Glu Lys Met Lys Ala Ser Glu Lys Ile Phe Tyr
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Val Tyr Met Lys Arg Lys Tyr Glu Ala Met Thr Lys Leu Gly Phe Lys
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Ala Thr Leu Pro Pro Phe Met Cys Asn Lys Arg Ala Glu Asp Phe Gln
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Gly Asn Asp Leu Asp Asn Asp Pro Asn Arg Gly Asn Gln Val Glu Arg
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Pro Lys Lys Pro Ala Glu Glu Gly Asn Asp Ser Glu Glu Val Pro Glu
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Ala Ser Gly Pro Gln Asn Asp Gly Lys Glu Leu Cys Pro Pro Gly Lys
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Pro Thr Thr Ser Glu Lys Ile His Glu Arg Ser Gly Pro Lys Arg Gly
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<213> Homo sapiens

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Val Lys Arg Arg Asp Ser Ala Thr Ser Phe Ser Leu Asp Phe Gly Tyr
 35 40 45

Leu Arg Asn Lys Asn Gly Cys His Val Glu Leu Leu Phe Leu Arg Tyr
 50 55 60

Ile Ser Asp Trp Asp Leu Asp Pro Gly Arg Cys Tyr Arg Val Thr Trp
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Phe Thr Ser Trp Ser Pro Cys Tyr Asp Cys Ala Arg His Val Ala Asp
 85 90 95

Phe Leu Arg Gly Asn Pro Asn Leu Ser Leu Arg Ile Phe Thr Ala Arg
 100 105 110

Leu Tyr Phe Cys Glu Asp Arg Lys Ala Glu Pro Glu Gly Leu Arg Arg
 115 120 125

Leu His Arg Ala Gly Val Gln Ile Ala Ile Met Thr Phe Lys Asp Tyr
 130 135 140

Phe Tyr Cys Trp Asn Thr Phe Val Glu Asn His Glu Arg Thr Phe Lys
 145 150 155 160

Ala Trp Glu Gly Leu His Glu Asn Ser Val Arg Leu Ser Arg Gln Leu
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Arg Arg Ile Leu Leu Pro Leu Tyr Glu Val Asp Asp Leu Arg Asp Ala
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Phe Arg Thr Leu Gly Leu
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<212> DNA

<213> Homo sapiens

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<210> 204

<211> 198

<212> PRT

<213> Homo sapiens

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Val Lys Arg Arg Asp Ser Ala Thr Ser Phe Ser Leu Asp Phe Gly Tyr
      35              40              45

Leu Arg Asn Lys Asn Gly Cys His Val Glu Leu Leu Phe Leu Arg Tyr
      50              55              60

Ile Ser Asp Trp Asp Leu Asp Pro Gly Arg Cys Tyr Arg Val Thr Trp
      65              70              75              80

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 Phe Leu Arg Gly Asn Pro Asn Leu Ser Leu Arg Ile Phe Thr Ala Arg
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 Leu Tyr Phe Cys Glu Asp Arg Lys Ala Glu Pro Glu Gly Leu Arg Arg
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 Leu His Arg Ala Gly Val Gln Ile Ala Ile Met Thr Phe Lys Asp Tyr
 130 135 140
 Phe Tyr Cys Trp Asn Thr Phe Val Glu Asn His Glu Arg Thr Phe Lys
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 Ala Trp Glu Gly Leu His Glu Asn Ser Val Arg Leu Ser Arg Gln Leu
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<212> DNA

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<210> 206

<211> 416

<212> PRT

<213> Homo sapiens

<400> 206

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Ser Ser Gly Tyr His Tyr Gly Val Ser Ala Cys Glu Gly Cys Lys Gly
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Phe Phe Arg Arg Ser Ile Gln Lys Asn Met Val Tyr Thr Cys His Arg
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Asp Lys Asn Cys Ile Ile Asn Lys Val Thr Arg Asn Arg Cys Gln Tyr
85 90 95

Cys Arg Leu Gln Lys Cys Phe Glu Val Gly Met Ser Lys Glu Ser Val
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Arg Asn Asp Arg Asn Lys Lys Lys Lys Glu Val Pro Lys Pro Glu Cys
115 120 125

Ser Glu Ser Tyr Thr Leu Thr Pro Glu Val Gly Glu Leu Ile Glu Lys
130 135 140

Val Arg Lys Ala His Gln Glu Thr Phe Pro Ala Leu Cys Gln Leu Gly
145 150 155 160

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Lys Tyr Thr Thr Asn Asn Ser Ser Glu Gln Arg Val Ser Leu Asp Ile
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 225 230 235 240
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 Gly Pro Leu Thr Asp Leu Val Phe Ala Phe Ala Asn Gln Leu Leu Pro
 260 265 270
 Leu Glu Met Asp Asp Ala Glu Thr Gly Leu Leu Ser Ala Ile Cys Leu
 275 280 285
 Ile Cys Gly Asp Arg Gln Asp Leu Glu Gln Pro Asp Arg Val Asp Met
 290 295 300
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 305 310 315 320
 Arg Pro Ser Arg Pro His Met Phe Pro Lys Met Leu Met Lys Ile Thr
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 Asp Leu Arg Ser Ile Ser Ala Lys Gly Ala Glu Arg Val Ile Thr Leu
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 Lys Met Glu Ile Pro Gly Ser Met Pro Pro Leu Ile Gln Glu Met Leu
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 Glu Asn Ser Glu Gly Leu Asp Thr Leu Ser Gly Gln Pro Gly Gly Gly
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<211> 1284

<212> DNA

<213> Homo sapiens

<400> 207

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gacaagaact gcatcatcaa caaggtgacc cggaaccgct gccagtactg ccgactgcag 300
aagtgccttg aagtgggcat gtccaaggag tctgtgagaa acgaccgaaa caagaagaag 360
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aagttcagtg aactctccac caagtgcac attagactg tggagttcgc caagcagctg 600
cccggcttca ccaccctcac catcgccgac cagatcacc tctcaaggc tgcctgcctg 660
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<211> 797

<212> PRT

<213> Homo sapiens

<400> 208

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Arg Gln Pro Ser Pro Ser Pro Ser Pro Thr Glu Arg Ala Pro Ala Ser
  35              40              45

Glu Glu Glu Phe Gln Phe Leu Arg Cys Gln Gln Cys Gln Ala Glu Ala
  50              55              60

Lys Cys Pro Lys Leu Leu Pro Cys Leu His Thr Leu Cys Ser Gly Cys
  65              70              75              80

Leu Glu Ala Ser Gly Met Gln Cys Pro Ile Cys Gln Ala Pro Trp Pro
          85              90              95

Leu Gly Ala Asp Thr Pro Ala Leu Asp Asn Val Phe Phe Glu Ser Leu
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Gln Arg Arg Leu Ser Val Tyr Arg Gln Ile Val Asp Ala Gln Ala Val
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Cys Thr Arg Cys Lys Glu Ser Ala Asp Phe Trp Cys Phe Glu Cys Glu
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Gln Leu Leu Cys Ala Lys Cys Phe Glu Ala His Gln Trp Phe Leu Lys
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His Glu Ala Arg Pro Leu Ala Glu Leu Arg Asn Gln Ser Val Arg Glu

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175

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Lys	Pro	Leu	Cys	Cys	Ser	Cys	Ala	Leu	Leu	Asp	Ser	Ser	His	Ser	Glu	
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Leu	Lys	Cys	Asp	Ile	Ser	Ala	Glu	Ile	Gln	Gln	Arg	Gln	Glu	Glu	Leu	
			225				230							235	240	
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Val	His	Ala	Gln	Met	His	Ala	Ala	Val	Gly	Gln	Leu	Gly	Arg	Ala	Arg	
			260													
Ala	Glu	Thr	Glu	Glu	Leu	Ile	Arg	Glu	Arg	Val	Arg	Gln	Val	Val	Ala	
			275													
His	Val	Arg	Ala	Gln	Glu	Arg	Glu	Leu	Leu	Glu	Ala	Val	Asp	Ala	Arg	
			290													
Tyr	Gln	Arg	Asp	Tyr	Glu	Glu	Met	Ala	Ser	Arg	Leu	Gly	Arg	Leu	Asp	
			305													
Ala	Val	Leu	Gln	Arg	Ile	Arg	Thr	Gly	Ser	Ala	Leu	Val	Gln	Arg	Met	
				325												
Lys	Cys	Tyr	Ala	Ser	Asp	Gln	Glu	Val	Leu	Asp	Met	His	Gly	Phe	Leu	
			340													
Arg	Gln	Ala	Leu	Cys	Arg	Leu	Arg	Gln	Glu	Glu	Pro	Gln	Ser	Leu	Gln	
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Ala	Ala	Val	Arg	Thr	Asp	Gly	Phe	Asp	Glu	Phe	Lys	Val	Arg	Leu	Gln	
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Asp	Leu	Ser	Ser	Cys	Ile	Thr	Gln	Gly	Lys	Ala	Ile	Glu	Thr	Gln	Ser	
			385													
Ser	Ser	Ser	Glu	Glu	Ile	Val	Pro	Ser	Pro	Pro	Ser	Pro	Pro	Pro	Leu	
Pro	Arg	Ile	Tyr	Lys	Pro	Cys	Phe	Val	Cys	Gln	Asp	Lys	Ser	Ser	Gly	
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			435													
Arg	Ser	Ile	Gln	Lys	Asn	Met	Val	Tyr	Thr	Cys	His	Arg	Asp	Lys	Asn	
			450													
Cys	Ile	Ile	Asn	Lys	Val	Thr	Arg	Asn	Arg	Cys	Gln	Tyr	Cys	Arg	Leu	
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 Asp Lys Phe Ser Glu Leu Ser Thr Lys Cys Ile Ile Lys Thr Val Glu
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 660 665 670
 Asp Arg Gln Asp Leu Glu Gln Pro Asp Arg Val Asp Met Leu Gln Glu
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 Pro Leu Leu Glu Ala Leu Lys Val Tyr Val Arg Lys Arg Arg Pro Ser
 690 695 700
 Arg Pro His Met Phe Pro Lys Met Leu Met Lys Ile Thr Asp Leu Arg
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 Ser Ile Ser Ala Lys Gly Ala Glu Arg Val Ile Thr Leu Lys Met Glu
 725 730 735
 Ile Pro Gly Ser Met Pro Pro Leu Ile Gln Glu Met Leu Glu Asn Ser
 740 745 750
 Glu Gly Leu Asp Thr Leu Ser Gly Gln Pro Gly Gly Gly Gly Arg Asp
 755 760 765
 Gly Gly Gly Leu Ala Pro Pro Pro Gly Ser Cys Ser Pro Ser Leu Ser
 770 775 780

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Pro Ser Ser Asn Arg Ser Ser Pro Ala Thr His Ser Pro
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 <212> DNA
 <213> Homo sapiens

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 <213> Homo sapiens

<400> 212
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Arg	Asn	Ser	Gln	His	Tyr	Thr	Leu	Asp	Phe	Leu	Ser	Pro	Lys	Thr	Phe	
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Gln	Gln	Ile	Leu	Glu	Tyr	Ala	Tyr	Thr	Ala	Thr	Leu	Gln	Ala	Lys	Ala	
85					90					95						
Glu	Asp	Leu	Asp	Asp	Leu	Leu	Tyr	Ala	Ala	Glu	Ile	Leu	Glu	Ile	Glu	
100					105					110						
Tyr	Leu	Glu	Glu	Gln	Cys	Leu	Lys	Met	Leu	Glu	Thr	Ile	Gln	Ala	Ser	
115					120					125						
Asp	Asp	Asn	Asp	Thr	Glu	Ala	Thr	Met	Ala	Asp	Gly	Gly	Ala	Glu	Glu	
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Glu	Glu	Asp	Arg	Lys	Ala	Arg	Tyr	Leu	Lys	Asn	Ile	Phe	Ile	Ser	Lys	
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His	Ser	Ser	Glu	Glu	Ser	Gly	Tyr	Ala	Ser	Val	Ala	Gly	Gln	Ser	Leu	
165					170					175						
Pro	Gly	Pro	Met	Val	Asp	Gln	Ser	Pro	Ser	Val	Ser	Thr	Ser	Phe	Gly	
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Leu	Ser	Ala	Met	Ser	Pro	Thr	Lys	Ala	Ala	Val	Asp	Ser	Leu	Met	Thr	
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Glu	Glu	Pro	Thr	Leu	Ala	Gly	Gly	Gly	Arg	His	Pro	Gly	Val	Ala	Glu	
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Val	Lys	Thr	Glu	Met	Met	Gln	Val	Asp	Glu	Val	Pro	Ser	Gln	Asp	Ser	
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Pro	Gly	Ala	Ala	Glu	Ser	Ser	Ile	Ser	Gly	Gly	Met	Gly	Asp	Lys	Val	
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Gln	Val	Pro	Pro	Pro	Ala	Glu	Ala	Gly	Gln	Ala	Pro	Thr	Gly	Arg	Pro	
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340					345					350						

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Thr Ser Gly Leu His Val Gln Pro Ala Leu Ala Val Ser Met Asp Phe
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 Ser Thr Tyr Gly Gly Leu Leu Pro Gln Gly Phe Ile Gln Arg Glu Leu
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 Phe Ser Lys Leu Gly Glu Leu Ala Val Gly Met Lys Ser Glu Ser Arg
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 Thr Ile Gly Glu Gln Cys Ser Val Cys Gly Val Glu Leu Pro Asp Asn
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 Gly Cys Glu Leu Cys Gly Lys Arg Phe Leu Asp Ser Leu Arg Leu Arg
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 Gln Cys Gly Ala Gln Phe Ser Lys Glu Asp Ala Leu Glu Thr His Arg
 465 470 475 480
 Gln Thr His Thr Gly Thr Asp Met Ala Val Phe Cys Leu Leu Cys Gly
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 Lys Arg Phe Gln Ala Gln Ser Ala Leu Gln Gln His Met Glu Val His
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 Ala Gly Val Arg Ser Tyr Ile Cys Ser Glu Cys Asn Arg Thr Phe Pro
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 Ser His Thr Ala Leu Lys Arg His Leu Arg Ser His Thr Gly Asp His
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 Pro Tyr Glu Cys Glu Phe Cys Gly Ser Cys Phe Arg Asp Glu Ser Thr
 545 550 555 560
 Leu Lys Ser His Lys Arg Ile His Thr Gly Glu Lys Pro Tyr Glu Cys
 565 570 575
 Asn Gly Cys Asp Lys Lys Phe Ser Leu Lys His Gln Leu Glu Thr His
 580 585 590
 Tyr Arg Val His Thr Gly Glu Lys Pro Phe Glu Cys Lys Leu Cys His
 595 600 605
 Gln Arg Ser Arg Asp Tyr Ser Ala Met Ile Lys His Leu Arg Thr His
 610 615 620
 Asn Gly Ala Ser Pro Tyr Gln Cys Thr Ile Cys Thr Glu Tyr Cys Pro
 625 630 635 640
 Ser Leu Ser Ser Met Gln Lys His Met Lys Gly His Lys Pro Glu Glu
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Ile Pro Pro Asp Trp Arg Ile Glu Lys Thr Tyr Leu Tyr Leu Cys Tyr
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Val

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 <212> DNA
 <213> Homo sapiens

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 <212> PRT
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<400> 214
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Pro Thr Gly Leu Leu Cys Lys Ala Asn Gln Met Arg Leu Ala Gly Thr	20	25	30
Leu Cys Asp Val Val Ile Met Val Asp Ser Gln Glu Phe His Ala His	35	40	45
Arg Thr Val Leu Ala Cys Thr Ser Lys Met Phe Glu Ile Leu Phe His	50	55	60
Arg Asn Ser Gln His Tyr Thr Leu Asp Phe Leu Ser Pro Lys Thr Phe	65	70	75
Gln Gln Ile Leu Glu Tyr Ala Tyr Thr Ala Thr Leu Gln Ala Lys Ala	85	90	95
Glu Asp Leu Asp Asp Leu Leu Tyr Ala Ala Glu Ile Leu Glu Ile Glu	100	105	110
Tyr Leu Glu Glu Gln Cys Leu Lys Met Leu Glu Thr Ile Gln Ala Ser	115	120	125
Asp Asp Asn Asp Thr Glu Ala Thr Met Ala Asp Gly Gly Ala Glu Glu	130	135	140
Glu Glu Asp Arg Lys Ala Arg Tyr Leu Lys Asn Ile Phe Ile Ser Lys	145	150	155
His Ser Ser Glu Glu Ser Gly Tyr Ala Ser Val Ala Gly Gln Ser Leu	165	170	175
Pro Gly Pro Met Val Asp Gln Ser Pro Ser Val Ser Thr Ser Phe Gly	180	185	190
Leu Ser Ala Met Ser Pro Thr Lys Ala Ala Val Asp Ser Leu Met Thr	195	200	205
Ile Gly Gln Ser Leu Leu Gln Gly Thr Leu Gln Pro Pro Ala Gly Pro	210	215	220
Glu Glu Pro Thr Leu Ala Gly Gly Gly Arg His Pro Gly Val Ala Glu	225	230	235
Val Lys Thr Glu Met Met Gln Val Asp Glu Val Pro Ser Gln Asp Ser	245	250	255
Pro Gly Ala Ala Glu Ser Ser Ile Ser Gly Gly Met Gly Asp Lys Val	260	265	270
Glu Glu Arg Gly Lys Glu Gly Pro Gly Thr Pro Thr Arg Ser Ser Val	275	280	285
Ile Thr Ser Ala Arg Glu Leu His Tyr Gly Arg Glu Glu Ser Ala Glu	290	295	300
Gln Val Pro Pro Pro Ala Glu Ala Gly Gln Ala Pro Thr Gly Arg Pro	305	310	315
			320

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Glu	His	Pro	Ala	Pro	Pro	Pro	Glu	Lys	His	Leu	Gly	Ile	Tyr	Ser	Val	325	330	335
Leu	Pro	Asn	His	Lys	Ala	Asp	Ala	Val	Leu	Ser	Met	Pro	Ser	Ser	Val	340	345	350
Thr	Ser	Gly	Leu	His	Val	Gln	Pro	Ala	Leu	Ala	Val	Ser	Met	Asp	Phe	355	360	365
Ser	Thr	Tyr	Gly	Gly	Leu	Leu	Pro	Gln	Gly	Phe	Ile	Gln	Arg	Glu	Leu	370	375	380
Phe	Ser	Lys	Leu	Gly	Glu	Leu	Ala	Val	Gly	Met	Lys	Ser	Glu	Ser	Arg	385	390	395
Thr	Ile	Gly	Glu	Gln	Cys	Ser	Val	Cys	Gly	Val	Glu	Leu	Pro	Asp	Asn	405	410	415
Glu	Ala	Val	Glu	Gln	His	Arg	Lys	Leu	His	Ser	Gly	Met	Lys	Thr	Tyr	420	425	430
Gly	Cys	Glu	Leu	Cys	Gly	Lys	Arg	Phe	Leu	Asp	Ser	Leu	Arg	Leu	Arg	435	440	445
Met	His	Leu	Leu	Ala	His	Ser	Ala	Gly	Ala	Lys	Ala	Phe	Val	Cys	Asp	450	455	460
Gln	Cys	Gly	Ala	Gln	Phe	Ser	Lys	Glu	Asp	Ala	Leu	Glu	Thr	His	Arg	465	470	475
Gln	Thr	His	Thr	Gly	Thr	Asp	Met	Ala	Val	Phe	Cys	Leu	Leu	Cys	Gly	485	490	495
Lys	Arg	Phe	Gln	Ala	Gln	Ser	Ala	Leu	Gln	Gln	His	Met	Glu	Val	His	500	505	510
Ala	Gly	Val	Arg	Ser	Tyr	Ile	Cys	Ser	Glu	Cys	Asn	Arg	Thr	Phe	Pro	515	520	525
Ser	His	Thr	Ala	Leu	Lys	Arg	His	Leu	Arg	Ser	His	Thr	Gly	Asp	His	530	535	540
Pro	Tyr	Glu	Cys	Glu	Phe	Cys	Gly	Ser	Cys	Phe	Arg	Asp	Glu	Ser	Thr	545	550	555
Leu	Lys	Ser	His	Lys	Arg	Ile	His	Thr	Gly	Glu	Lys	Pro	Tyr	Glu	Cys	565	570	575
Asn	Gly	Cys	Asp	Lys	Lys	Phe	Ser	Leu	Lys	His	Gln	Leu	Glu	Thr	His	580	585	590
Tyr	Arg	Val	His	Thr	Gly	Glu	Lys	Pro	Phe	Glu	Cys	Lys	Leu	Cys	His	595	600	605
Gln	Arg	Ser	Arg	Asp	Tyr	Ser	Ala	Met	Ile	Lys	His	Leu	Arg	Thr	His	610	615	620

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Asn Gly Ala Ser Pro Tyr Gln Cys Thr Ile Cys Thr Glu Tyr Cys Pro
 625 630 635 640

Ser Leu Ser Ser Met Gln Lys His Met Lys Gly His Lys Pro Glu Glu
 645 650 655

Ile Pro Pro Asp Trp Arg Ile Glu Lys Thr Tyr Leu Tyr Leu Cys Tyr
 660 665 670

Val

<210> 215

<211> 2197

<212> DNA

<213> Homo sapiens

<400> 215

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gccgagggga gcaccatgga tctgacaaaa atgggcatga tccagctgca gaaccctagc 120
caccacacgg ggctactgtg caaggccaac cagatgcggc tggccgggac tttgtgcgat 180
gtggtcatca tgggtggacag ccaggagtgc cacgcccacc ggacggtgct ggcctgcacc 240
agcaagatgt ttgagatcct cttccaccgc aatagtcaac actatacttt ggacttcctc 300
tcgccaaaga ctttccagca gattctggag tatgcatata cagccacgct gcaagccaag 360
gcggaggacc tggatgacct gctgtatgcg gccgagatcc tggagatcga gtacctggag 420
gaacagtgcc tgaagatgct ggagaccatc caggcctcag acgacaatga cacggaggcc 480
accatggccg atggcgggggc cgaggaagaa gaggaccgca aggctcggta cctcaagaac 540
atcttcatct cgaagcattc cagcgaggag agtgggtatg ccagtgtggc tggacagagc 600
ctccctgggc ccatggtgga ccagagccct tcagtctcca cttcatttgg tctttcagcc 660
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cctgggggtg ctgaggtgaa gacggagatg atgcagggtg atgaggtgcc cagccaggac 840
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aagtcagaga gccggaccat cggagagcag tgcagcgtgt gtggggtcga gcttcctgat 1320
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cacacagggtg agaagccctt tgagtgtgaa ctctgccacc agcgtcccc ggactactcg 1920
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acagagtact gcccagcct ctcctccatg cagaagcaca tgaagggcca caagcccagag 2040
gagatcccgc ccgactggag gatagagaag acgtacctct acctgtgcta tgtgtgaagg 2100
gaggcccgcg gcggtggagc cgagcgggga gccaggaaag aagagttgga gtgagatgaa 2160
ggaaggacta tgacaaataa aaaaaaaaaa ggaattc 2197

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<210> 216

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<211> 29

<212> PRT

<213> Homo sapiens

<400> 216

Arg Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Glu
1 5 10 15

Leu Leu Gln Glu Glu Thr Arg Gln Lys Leu Asn Val Ser
20 25

<210> 217

<211> 89

<212> DNA

<213> Homo sapiens

<400> 217

acgcgaattt gaagatagag acaggtctca tcgggaggaa atggaggagc tgcttcaaga 60
agaaaccgg cagaagctca acgtgtcta 89

<210> 218

<211> 26

<212> PRT

<213> Homo sapiens

<400> 218

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Phe Lys
1 5 10 15

Arg Ala Lys Ala Asn Leu Asp Lys Asn Lys
20 25

<210> 219

<211> 78

<212> DNA

<213> Homo sapiens

<400> 219

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aacctagaca agaataag 78

<210> 220

<211> 34

<212> PRT

<213> Homo sapiens

<400> 220

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Val His
1 5 10 15

Glu Leu Glu Lys Ser Lys Arg Ala Leu Glu Thr Gln Met Glu Glu Met
20 25 30

Lys Thr

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<210> 221
<211> 102
<212> DNA
<213> Homo sapiens

<400> 221
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tccaagcggg ccctggagac ccagatggag gagatgaaga cg 102

<210> 222
<211> 50
<212> PRT
<213> Homo sapiens

<400> 222
Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Asn Glu
1 5 10 15
Val Glu Ser Val Thr Gly Met Leu Asn Glu Ala Glu Gly Lys Ala Ile
20 25 30
Lys Leu Ala Lys Asp Val Ala Ser Leu Ser Ser Gln Leu Gln Asp Thr
35 40 45
Gln Glu
50

<210> 223
<211> 152
<212> DNA
<213> Homo sapiens

<400> 223
gaatttgaag atagagacag gtctcatcgg gaggaatgg agaatgaagt tgagagcgtc 60
acaggggatgc ttaacgaggc cgagggggaag gccattaagc tggccaagga cgtggcgtcc 120
ctcagttccc agctccagga caccagaggag tt 152

<210> 224
<211> 1353
<212> DNA
<213> Homo sapiens

<220>
<221> modified_base
<222> (941)
<223> a, c, t, g, other or unknown

<220>
<221> modified_base
<222> (1067)
<223> a, c, t, g, other or unknown

<220>

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<221> modified_base

<222> (1077)

<223> a, c, t, g, other or unknown

<400> 224

cttggccaac	attctggagg	cagtaaagaa	agcttataga	ataaccacat	attagaactt	60
gtgaaggaga	aaatatacat	atatatatat	gtatatatat	agtctctcta	ttaagtaatt	120
taccataagg	ggtttaaata	ggaatgtttt	ctccaaagtg	aatcttgaaa	tcttggtggt	180
tataattgtc	aagcctcttt	ttttaaaata	gatttgggtca	acaggaagta	tttttttcta	240
atthtttattt	tatagaccta	gtcaagcttc	ttaattgtta	aatattgtta	taacaataca	300
tctgggcccgg	gcgcggtggc	tcactcctgt	aatcccagca	ctttgggagg	ccagggcggg	360
tgaatcacga	ggtcaggaga	ttgagaccat	cctggctaac	acaaagaaac	cccatctcta	420
ctaaaaatac	aaaaaattag	ctgggagagg	aggagggcgc	ctgtagtccc	agctactcgg	480
gaggcgggagc	ttgcggtgag	ccaagatcgc	gccactgcac	tccagcgact	ccgtctcaaa	540
aaaaaaaaaa	aaaaaacatc	tgagtcggta	catggttggt	agccgaggag	aaaaacatct	600
cttccaaata	cgcggtatgag	aggacagag	ctgaggcaga	agccagggag	aaggaaacca	660
aggccctgtc	cctggctcgg	gcccttgaag	aggccttgga	agccaaagag	gaactcgagc	720
ggaccaacaa	aatgctcaaa	gccgaaatgg	aagacctggt	cagctccaag	gatgacgtgg	780
gcaagaacgt	aagtggctct	gggtgggttt	tctcgtccat	gtttcgcctg	cccaccctct	840
gtgctattca	ccagtcctatg	cgaggctagc	tccctggcctt	tttcatagcg	aactatcatc	900
ggaaatggaa	ggaggttttt	ggactgggtc	aggggcta	naggggctga	gaatggcagt	960
cgaggatggg	tctgagttgg	gggtccgag	gataaggctg	gggtctgaac	tctcaggggt	1020
catcttgagt	cccgcccatg	catcctgtgg	gaggccaaag	ccacctnccc	tgatctncc	1080
gaggtgccgc	tcacggtggg	tttctcaatc	gtcttcatga	agttgagcct	catagaatgg	1140
ggctgcccgc	tctgccggca	ggtccatgag	ctggagaagt	ccaagcgggc	cctggagacc	1200
cagatggagg	agatgaagac	gcagctggaa	gagctggagg	acgagctgca	agccacggag	1260
gacgccaaac	tgcggtctga	agtcaacatg	caggcgctca	agggccagtt	cgaagggat	1320
ctccaagccc	gggacgagca	gaatgaggag	aag			1353

<210> 225

<211> 744

<212> DNA

<213> Homo sapiens

<220>

<221> modified_base

<222> (326)

<223> a, c, t, g, other or unknown

<220>

<221> modified_base

<222> (614)

<223> a, c, t, g, other or unknown

<400> 225

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taatctaata	ggctgatagc	agctgaggat	gtccccaaga	atacttgta	gctaagagaa	120
gaaaatggag	ggatatatgt	gatacttggt	ttctttgatg	ctggttgta	tcttggtgatt	180
ttcatatatg	tgaatacaag	acttccacac	catgcccttt	ctttcggtat	ctgtaaaatt	240
tagaagcttt	aaaatgtata	atgtacattt	gttacatttc	tgaacctttt	tgctcatgct	300
ctttgttccc	tgatgtagaa	tgttcnatc	tgtccgtcaa	ggcccaacct	gaatgttgct	360
attaaatgtc	aggcctttcc	tcagtctctg	gggtctgaac	tgctcagggg	tcactcttag	420
tcccggccat	gcatcctgtg	ggaggccaaa	gccacctccc	tgatctcctg	aggtgccgct	480
cacggtgggt	ttctcaatcg	tcttcatgaa	gttgagcctc	atagaatggg	gctgcccgct	540
ctgccggcag	gtccatgagc	tggagaagtc	caagcgggac	ctggagaccc	agatggagga	600
gatgaagacg	cagntggaag	agctggagga	cgagctgcaa	gccacggagg	acgccaaact	660
gcggctggaa	gtcaacatgc	aggcgctcaa	gggccagttc	gaaagggatc	tccaagcccc	720

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ggacgagcag aatgaggaga agag

744

<210> 226

<211> 60

<212> DNA

<213> Homo sapiens

<400> 226

tctctgtgcc agtagtgggc atgtagagga ccctaataagg agtattcata ccagcagcag 60

<210> 227

<211> 25

<212> PRT

<213> Homo sapiens

<400> 227

Met	Pro	Arg	Phe	Gly	Phe	Gln	Ile	Gly	Val	Arg	Tyr	Glu	Asn	Lys	Lys
1				5				10					15		

Arg	Glu	Asn	Leu	Ala	Leu	Thr	Leu	Leu
			20				25	

<210> 228

<211> 300

<212> DNA

<213> Homo sapiens

<400> 228

agctctcctt	gcagcccgag	ctgaccctag	gcctccaccc	tggcaggaat	cccaatttgc	60
ctccacttag	tgagcggaag	aatgtgctac	agttgaaact	ccagcagcgc	cggacccggg	120
aagaactggg	gagccaaggg	atcatgccgc	ggtttggttt	tcagatagga	gtaggtatg	180
agaacaagaa	gagagaaaac	ttggcgctga	ccctgttata	gtggttatag	tggtgtccct	240
aaagggagga	aatgatttca	gcaaaactgg	ttgaacagcg	gatgaagata	tggaattcaa	300

<210> 229

<211> 43

<212> PRT

<213> Homo sapiens

<400> 229

Lys	Met	Arg	Lys	Met	Glu	Asp	Asn	Gln	Tyr	Ser	Glu	Ala	Glu	Leu	Ser
1				5				10					15		

Ser	Phe	Ser	Thr	Ser	His	Val	Pro	Glu	Glu	Leu	Lys	Gln	Pro	Leu	His
			20					25					30		

Arg	Lys	Ser	Lys	Ser	Gln	Val	Gln	Ile	Phe	Pro
			35				40			

<210> 230

<211> 916

<212> DNA

<213> Homo sapiens

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<400> 230

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aaaatgagga aaatggaaga taatcaatat tctgaagctg agctgtcttc ttttagtact 60
tcccatgtgc cagaggaact taagcagccg ttacacagaa agtccaaatc gcaggtagag 120
attttcccat agtacagcat catgggttaca ttatgcatga aacgtacatt tcctttgatt 180
accaaaaaagc aaatattcta tctttgaaat attttagaat ccaaatgggg tcagatgcct 240
ttctaaaaat gttcatatct ttactgtatt tatgaccaa tccaaaatag ttaagcaaga 300
aagcaattaa tttagctgca ttctgtatag aaattttatg acaagcccca tcctacactt 360
atctttcctt gactttgcaa ttctcttact tttgtacagt tagttcatca tgtttgttta 420
caaataattta tgtattacct cagagtcatt ttccgtgtct atactttttg tcaatgtaat 480
tatattttta gatttttctg aaaagtgaat tctatttttt gtccccttct atgtctagta 540
aattgtagg ttagtgaat tagcaagtca tctcatgttg taatttaata gtaaaatgag 600
gatcagcaag gaagtgaatt gccaaagggtc tacaccaact tactggcaga ttgggaaata 660
aaacctgtca atttaaattc aacaaatgaa tgagtgaatg aatggtactc aaatttatta 720
ggctctacaa cattgtatca gcactatggg aactaaaaat aaatctattt aagggtccat 780
aaatagcaat taaaagagcc tcagtgtttt tgttacaaaa taaaggaagt cgggtactttt 840
ttgtttgaca tccacactca accggattgt tcattcaggt caattaaaaa taaagaaact 900
tcctattacc aaaaaa 916

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<210> 231

<211> 268

<212> PRT

<213> Homo sapiens

<400> 231

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Met Phe Arg Met Leu Asn Ser Ser Phe Glu Asp Asp Pro Phe Phe Ser
 1             5             10             15

Glu Ser Ile Leu Ala His Arg Glu Asn Met Arg Gln Met Ile Arg Ser
          20             25             30

Phe Ser Glu Pro Phe Gly Arg Asp Leu Leu Ser Ile Ser Asp Gly Arg
          35             40             45

Gly Arg Ala His Asn Arg Arg Gly His Asn Asp Gly Glu Asp Ser Leu
          50             55             60

Thr His Thr Asp Val Ser Ser Phe Gln Thr Met Asp Gln Met Val Ser
          65             70             75             80

Asn Met Arg Asn Tyr Met Gln Lys Leu Glu Arg Asn Phe Gly Gln Leu
          85             90             95

Ser Val Asp Pro Asn Gly His Ser Phe Cys Ser Ser Ser Val Met Thr
          100             105             110

Tyr Ser Lys Ile Gly Asp Glu Pro Pro Lys Val Phe Gln Ala Ser Thr
          115             120             125

Gln Thr Arg Arg Ala Pro Gly Gly Ile Lys Glu Thr Arg Lys Ala Met
          130             135             140

Arg Asp Ser Asp Ser Gly Leu Glu Lys Met Ala Ile Gly His His Ile
          145             150             155             160

His Asp Arg Ala His Val Ile Lys Lys Ser Lys Asn Lys Lys Thr Gly
          165             170             175

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Asp Glu Glu Val Asn Gln Glu Phe Ile Asn Met Asn Glu Ser Asp Ala
 180 185 190

His Ala Phe Asp Glu Glu Trp Gln Ser Glu Val Leu Lys Tyr Lys Pro
 195 200 205

Gly Arg His Asn Leu Gly Asn Thr Arg Met Arg Ser Val Gly His Glu
 210 215 220

Asn Pro Gly Ser Arg Glu Leu Lys Arg Arg Glu Lys Pro Gln Gln Ser
 225 230 235 240

Pro Ala Ile Glu His Gly Arg Arg Ser Asn Val Leu Gly Asp Lys Leu
 245 250 255

His Ile Lys Gly Ser Ser Val Lys Ser Asn Lys Lys
 260 265

<210> 232

<211> 1116

<212> DNA

<213> Homo sapiens

<400> 232

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gttatgtggt cccgtccgta ctggaggcta gctcttgctg cggccgcggc gagttaacat 60
cgttttttcca atctgtccgc ggctgcccgc acccaagaca gagccagaat gttcaggatg 120
ctgaacagca gttttgagga tgaccccttc ttctctgagt ccattcttgc acaccgagaa 180
aatatgcgac agatgataag aagtttttct gaaccctttg gaagagactt gctcagtatc 240
tctgatggta gagggagagc tcataatcgt agaggacata atgatggtga agattctttg 300
actcatacag atgtcagctc tttccagacc atggaccaa tgggtgtcaaa tatgagaaac 360
tatatgcaga aattagaaag aaacttcggt caactttcag tggatccaaa tggacattca 420
ttttgttctt cctcagttat gacttattcc aaaataggag atgaaccgcc aaagggtttt 480
caggcctcaa ctcaaactcg tcgagctcca ggaggaataa aggaaaccag gaaagcaatg 540
agagattctg acagtggact agaaaaaatg gctattggtc atcatatcca tgaccgagct 600
catgtcatta aaaagtcaaa gaacaagaag actggagatg aagagggtcaa ccaggagtgc 660
atcaatatga atgaaagcga tgctcatgct tttgatgagg agtggcaaag tgagggtttg 720
aagtacaaac caggacgaca caatctagga aacactagaa tgagaagtgt tggccatgag 780
aatcctggct ccgagaact taaaagaagg gagaaaccc aacaaagtcc agccattgaa 840
catggaagga gatcaaatgt tttgggggac aaactccaca tcaaaggctc atctgtgaaa 900
agcaacaaaa aataaatagc catgcatttg atttgtttag ttttgattgt tttaacagtt 960
agtaatgggt ctgggtaata agcataagac caatctcttg ctgttaaata agttctgtcc 1020
ttggcaactt tcttctgata tctgaatgtt catgaaggct ctagctttat attgtccctc 1080
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<210> 233

<211> 268

<212> PRT

<213> Homo sapiens

<400> 233

Met Phe Arg Met Leu Asn Ser Ser Phe Glu Asp Asp Pro Phe Phe Ser
 1 5 10 15

Glu Ser Ile Leu Ala His Arg Glu Asn Met Arg Gln Met Ile Arg Ser
 20 25 30

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Phe Ser Glu Pro Phe Gly Arg Asp Leu Leu Ser Ile Ser Asp Gly Arg
 35 40 45
 Gly Arg Ala His Asn Arg Arg Gly His Asn Asp Gly Glu Asp Ser Leu
 50 55 60
 Thr His Thr Asp Val Ser Ser Phe Gln Thr Met Asp Gln Met Val Ser
 65 70 75 80
 Asn Met Arg Asn Tyr Met Gln Lys Leu Glu Arg Asn Phe Gly Gln Leu
 85 90 95
 Ser Val Asp Pro Asn Gly His Ser Phe Cys Ser Ser Ser Val Met Thr
 100 105 110
 Tyr Ser Lys Ile Gly Asp Glu Pro Pro Lys Val Phe Gln Ala Ser Thr
 115 120 125
 Gln Thr Arg Arg Ala Pro Gly Gly Ile Lys Glu Thr Arg Lys Ala Met
 130 135 140
 Arg Asp Ser Asp Ser Gly Leu Glu Lys Met Ala Ile Gly His His Ile
 145 150 155 160
 His Asp Arg Ala His Val Ile Lys Lys Ser Lys Asn Lys Lys Thr Gly
 165 170 175
 Asp Glu Glu Val Asn Gln Glu Phe Ile Asn Met Asn Glu Ser Asp Ala
 180 185 190
 His Ala Phe Asp Glu Glu Trp Gln Ser Glu Val Leu Lys Tyr Lys Pro
 195 200 205
 Gly Arg His Asn Leu Gly Asn Thr Arg Met Arg Ser Val Gly His Glu
 210 215 220
 Asn Pro Gly Ser Arg Glu Leu Lys Arg Arg Glu Lys Pro Gln Gln Ser
 225 230 235 240
 Pro Ala Ile Glu His Gly Arg Arg Ser Asn Val Leu Gly Asp Lys Leu
 245 250 255
 His Ile Lys Gly Ser Ser Val Lys Ser Asn Lys Lys
 260 265

<210> 234

<211> 1130

<212> DNA

<213> Homo sapiens

<400> 234

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<213> Homo sapiens

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Asn Met Arg Asn Tyr Met Gln Lys Leu Glu Arg Asn Phe Gly Gln Leu
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Ser Val Asp Pro Asn Gly His Ser Phe Cys Ser Ser Ser Val Met Thr
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Tyr Ser Lys Ile Gly Asp Glu Pro Pro Lys Val Phe Gln Ala Ser Thr
      115            120            125

Gln Thr Arg Arg Ala Pro Gly Gly Ile Lys Glu Thr Arg Lys Ala Met
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Arg Asp Ser Asp Ser Gly Leu Glu Lys Met Ala Ile Gly His His Ile
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His Asp Arg Ala His Val Ile Lys Lys Ser Lys Asn Lys Lys Thr Gly
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Asp Glu Glu Val Asn Gln Glu Phe Ile Asn Met Asn Glu Ser Asp Ala
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Asn Pro Gly Ser Arg Glu Leu Lys Arg Arg Glu Lys Pro Gln Gln Ser
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<212> DNA

<213> Homo sapiens

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<213> Homo sapiens

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Glu Asn Glu Ser Gly Gly Asp Lys Pro Pro Ile Asp Pro Asn Asn Pro
 35 40 45

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Ala Ala Asn Trp Leu His Ala Arg Ser Thr Arg Lys Lys Arg Cys Pro
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Tyr Thr Lys His Gln Thr Leu Glu Leu Glu Lys Glu Phe Leu Phe Asn
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Met Tyr Leu Thr Arg Asp
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 <212> DNA
 <213> Homo sapiens

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 <212> PRT
 <213> Homo sapiens

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 35 40 45

Thr Thr Leu Pro Phe Ile Thr Ser Val Glu Ile Val Ser Arg Tyr Leu
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Cys Ala Arg Gly Ser Gly Arg Ala Gly His His Gly Pro Gly Arg Ala
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Arg Pro Ala Val Ala Thr Ser Ala Phe Pro Ala Gln Glu Pro Arg Val
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Phe Leu Arg Ser Ala Leu Pro Ala Gly Arg Leu Ser Pro Ser Thr Thr
 100 105 110

His Leu His Leu Val Thr Ala Asp Asn Pro Ala Ala Asn Trp Leu His
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Thr	Thr	Leu	Pro	Phe	Ile	Thr	Ser	Val	Glu	Ile	Val	Ser	Arg	Tyr	Leu
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Phe	Leu	Arg	Ser	Ala	Leu	Pro	Ala	Gly	Arg	Leu	Ser	Pro	Ser	Thr	Thr
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Asp Arg Ala Lys Asp Glu
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Phe Ser Pro Cys Ser Phe Gln Ser Lys Ala Thr Val Phe Gly Ala Ser
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Trp Asn Pro Val His Ala Arg Ala Pro Thr Leu Tyr Pro Leu Val Tyr
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His His His His His His Pro Tyr Val His Pro Gln Ala Pro Trp Arg
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Arg Gly Ala Asp Gly Arg Tyr Met Arg Ser Cys Trp Ser Pro Thr Pro
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Gly Ala Leu Ser Phe Ala Gly Leu Pro Ser Ser Arg Pro Tyr Gly Ile
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Lys Pro Glu Pro Leu Ser Ala Arg Arg Gly Asp Cys Pro Thr Leu Asp
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Thr His Thr Phe Ser Leu Thr Asp Tyr Ala Cys Gly Ser Pro Pro Val
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Glu Asn Glu Ser Gly Gly Asp Lys Pro Pro Ile Asp Pro Asn Asn Pro
 180 185 190

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Ala Ala Asn Trp Leu His Ala Arg Ser Thr Arg Lys Lys Arg Cys Pro
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Tyr Thr Lys His Gln Thr Leu Glu Leu Glu Lys Glu Phe Leu Phe Asn
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Met Tyr Leu Thr Arg Asp Arg Arg Tyr Glu Val Ala Arg Leu Leu Asn
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<212> DNA

<213> Homo sapiens

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atatattttt aaaaatctac ctgttcctga cttaaaacaa aaggaaagaa actacctttt 6480
tataatgcac aactgttgat ggtaggctgt atagttttta gtctgtgtag ttaatttaat 6540
ttgcagtttg tgcggcagat tgctctgcca agatacttga acactgtgtt ttattgtggg 6600
aattatgttt tgtgattcaa acttctgtgt actgggtgat gcaccattg tgattgtgga 6660
agatagaatt c 6671

```

<210> 244

<211> 76

<212> PRT

<213> Homo sapiens

<400> 244

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Arg Pro Met Pro Arg Leu Glu Pro Thr Phe Glu Ile Asp Glu Glu Glu
 1             5             10             15
Glu Glu Glu Asp Glu Asn Glu Leu Phe Pro Arg Glu Tyr Phe Arg Arg
          20             25             30
Leu Ser Ser Gln Asp Val Leu Arg Cys Gln Ser Ser Ser Lys Arg Lys
          35             40             45
Ser Lys Asp Glu Glu Glu Asp Glu Glu Ser Asp Asp Ala Asp Asp Gly
          50             55             60
Asn Asn Trp Glu His Lys Ser Ile Trp Thr Ala Leu
          65             70             75

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<210> 245

<211> 415

<212> DNA

<213> Homo sapiens

<400> 245

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gaggccaatg ccaagattag aaccacatt tgagatcgat gaagaagagg aggaagagga 60
tgaaaatgaa cttttcccta gagaatactt ccgtcgtttg tcttcgcagg atgtactcag 120
gtgtcagtc tcttctaaga ggaagtctaa agatgaagaa gaagatgaag agtcagatga 180
tgctgatgat gggaataact gggaacacaa gtccatttgg acagcccttt agtcaagctg 240
gagggcagcc aatgggagcc actggagtga acccccagtt agccagcaaa cagagcatgg 300
tcaacagttt gccaccttc cctacagata tcaagaatac ttcagtcacc aacgtgccaa 360
atatgtctca gatgcaaaca tcagtgggaa ttgtaccac acaagcaatt gcaac 415

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<210> 246

<211> 68

<212> PRT

<213> Homo sapiens

<400> 246

Met Ala Glu Asn Leu Leu Asp Gly Pro Pro Asn Pro Lys Arg Ala Lys
 1 5 10 15

Leu Ser Ser Pro Gly Phe Ser Ala Asn Asp Ser Thr Asp Thr Pro Ile
 20 25 30

Leu Lys Pro Val Ser Leu Leu Arg Lys Arg Asp Val Lys Asn Ser Pro
 35 40 45

Leu Glu Pro Asp Thr Ser Thr Pro Leu Lys Lys Lys Lys Gly Trp Pro
 50 55 60

Lys Gly Lys Ser
 65

<210> 247

<211> 229

<212> DNA

<213> Homo sapiens

<400> 247

gggctgtttt cgcgagcagg tgaaaatggc tgagaacttg ctggacggac cgcccaaccc 60
 caaaaagagcc aaactcagct cgcccggttt ctcggcgaat gacagcacag acactcctat 120
 cttaaagcca gtatctcttt tgcgaaaacg tgatgtgaag aattctcctc ttgagccaga 180
 tacatccaca cttttgaaaa agaaaaaggg atggcccaaa ggcaagagc 229

<210> 248

<211> 376

<212> PRT

<213> Homo sapiens

<400> 248

Arg Pro Met Pro Arg Leu Glu Pro Thr Phe Glu Ile Asp Glu Glu Glu
 1 5 10 15

Glu Glu Glu Asp Glu Asn Glu Leu Phe Pro Arg Glu Tyr Phe Arg Arg
 20 25 30

Leu Ser Ser Gln Asp Val Leu Arg Cys Gln Ser Ser Ser Lys Arg Lys
 35 40 45

Ser Lys Asp Glu Glu Glu Asp Glu Glu Ser Asp Asp Ala Asp Asp Phe
 50 55 60

Gly Ser Leu Phe Asp Leu Glu Asn Asp Leu Pro Asp Glu Leu Ile Pro
 65 70 75 80

Asn Gly Gly Glu Leu Gly Leu Leu Asn Ser Gly Asn Leu Val Pro Asp
 85 90 95

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Ala Ala Ser Lys His Lys Gln Leu Ser Glu Leu Leu Arg Gly Gly Ser
 100 105 110
 Gly Ser Ser Ile Asn Pro Gly Ile Gly Asn Val Ser Ala Ser Ser Pro
 115 120 125
 Val Gln Gln Gly Leu Gly Gly Gln Ala Gln Gly Gln Pro Asn Ser Ala
 130 135 140
 Asn Met Ala Ser Leu Ser Ala Met Gly Lys Ser Pro Leu Ser Gln Gly
 145 150 155 160
 Asp Ser Ser Ala Pro Ser Leu Pro Lys Gln Ala Ala Ser Thr Ser Gly
 165 170 175
 Pro Thr Pro Ala Ala Ser Gln Ala Leu Asn Pro Gln Ala Gln Lys Gln
 180 185 190
 Val Gly Leu Ala Thr Ser Ser Pro Ala Thr Ser Gln Thr Gly Pro Gly
 195 200 205
 Ile Cys Met Asn Ala Asn Phe Asn Gln Thr His Pro Gly Leu Leu Asn
 210 215 220
 Ser Asn Ser Gly His Ser Leu Ile Asn Gln Ala Ser Gln Gly Gln Ala
 225 230 235 240
 Gln Val Met Asn Gly Ser Leu Gly Ala Ala Gly Arg Gly Arg Gly Ala
 245 250 255
 Gly Met Pro Tyr Pro Thr Pro Ala Met Gln Gly Ala Ser Ser Ser Val
 260 265 270
 Leu Ala Glu Thr Leu Thr Gln Val Ser Pro Gln Met Thr Gly His Ala
 275 280 285
 Gly Leu Asn Thr Ala Gln Ala Gly Gly Met Ala Lys Met Gly Ile Thr
 290 295 300
 Gly Asn Thr Ser Pro Phe Gly Gln Pro Phe Ser Gln Ala Gly Gly Gln
 305 310 315 320
 Pro Met Gly Ala Thr Gly Val Asn Pro Gln Leu Ala Ser Lys Gln Ser
 325 330 335
 Met Val Asn Ser Leu Pro Thr Phe Pro Thr Asp Ile Lys Asn Thr Ser
 340 345 350
 Val Thr Asn Val Pro Asn Met Ser Gln Met Gln Thr Ser Val Gly Ile
 355 360 365
 Val Pro Thr Gln Ala Ile Ala Thr
 370 375

<210> 249

<211> 1128

<212> DNA

189/299

<213> Homo sapiens

<400> 249

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gtgtcagtc tcttctaaga ggaagtctaa agatgaagaa gaagatgaag agtcagatga 180
tgctgatgat tttggatcat tgtttgactt ggaaaatgat cttcctgatg agctgatacc 240
caatggagga gaattaggcc ttttaaacag tgggaacctt gttccagatg ctgcttccaa 300
acataaacia ctgtcggagc ttctacgagg aggcagcggc tctagtatca acccaggaat 360
aggaaatgtg agcgccagca gccccgtgca gcagggcctg ggtggccagg ctcaagggca 420
gccgaacagt gctaacatgg ccagcctcag tgccatgggc aagagccctc tgagccaggg 480
agattcttca gccccagcc tgcctaaaca ggcagccagc acctctgggc ccaccccgcc 540
tgcctcccaa gcaactgaatc cgcaagcaca aaagcaagtg gggctggcga ctagcagccc 600
tgccacgtca cagactggac ctggtatctg catgaatgct aactttaacc agaccacccc 660
aggcctctc aatagtaact ctggccatag ctttaattaat caggcttcac aagggcaggc 720
gcaagtcatg aatggatctc ttggggctgc tggcagagga aggggagctg gaatgccgta 780
ccctactcca gccatgcagg gcgcctcgag cagcgtgctg gctgagaccc taacgcaggt 840
ttccccgcaa atgactggtc acgcgggact gaacaccgca caggcaggag gcatggccaa 900
gatgggaata actgggaaca caagtccact tggacagccc tttagtcaag ctggagggca 960
gccaatggga gccactggag tgaaccccca gttagccagc aaacagagca tggtaacag 1020
tttgcaccac ttccctacag atatcaagaa tacttcagtc accaacgtgc caaatatgtc 1080
tcagatgcaa acatcagtgg gaattgtacc cacacaagca attgcaac 1128

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<210> 250

<211> 2004

<212> PRT

<213> Homo sapiens

<400> 250

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Met Val Lys Leu Ala Asn Pro Leu Tyr Thr Glu Trp Ile Leu Glu Ala
  1              5              10              15

Ile Lys Lys Val Lys Lys Gln Lys Gln Arg Pro Ser Glu Glu Arg Ile
      20              25              30

Cys Asn Ala Val Ser Ser Ser His Gly Leu Asp Arg Lys Thr Val Leu
      35              40              45

Glu Gln Leu Glu Leu Ser Val Lys Asp Gly Thr Ile Leu Lys Val Ser
      50              55              60

Asn Lys Gly Leu Asn Ser Tyr Lys Asp Pro Asp Asn Pro Gly Arg Ile
      65              70              75              80

Ala Leu Pro Lys Pro Arg Asn His Gly Lys Leu Asp Asn Lys Gln Asn
      85              90              95

Val Asp Trp Asn Lys Leu Ile Lys Arg Ala Val Glu Gly Leu Ala Glu
      100             105             110

Ser Gly Gly Ser Thr Leu Lys Ser Ile Glu Arg Phe Leu Lys Gly Gln
      115             120             125

Lys Asp Val Ser Ala Leu Phe Gly Gly Ser Ala Ala Ser Gly Phe His
      130             135             140

Gln Gln Leu Arg Leu Ala Ile Lys Arg Ala Ile Gly His Gly Arg Leu

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145		150		155		160
Leu Lys Asp Gly Pro	Leu Tyr Arg Leu Asn Thr Lys Ala Thr Asn Val					
	165		170			175
Asp Gly Lys Glu Ser Cys Glu Ser Leu Ser Cys Leu Pro Pro Val Ser						
	180		185			190
Leu Leu Pro His Glu Lys Asp Lys Pro Val Ala Glu Pro Ile Pro Ile						
	195		200			205
Cys Ser Phe Cys Leu Gly Thr Lys Glu Gln Asn Arg Glu Lys Lys Pro						
	210		215			220
Glu Glu Leu Ile Ser Cys Ala Asp Cys Gly Asn Ser Gly His Pro Ser						
	225		230			235
Cys Leu Lys Phe Ser Pro Glu Leu Thr Val Arg Val Lys Ala Leu Arg						
	245		250			255
Trp Gln Cys Ile Glu Cys Lys Thr Cys Ser Ser Cys Arg Asp Gln Gly						
	260		265			270
Lys Asn Ala Asp Asn Met Leu Phe Cys Asp Ser Cys Asp Arg Gly Phe						
	275		280			285
His Met Glu Cys Cys Asp Pro Pro Leu Thr Arg Met Pro Lys Gly Met						
	290		295			300
Trp Ile Cys Gln Ile Cys Arg Pro Arg Lys Lys Gly Arg Lys Leu Leu						
	305		310			315
Gln Lys Lys Ala Ala Gln Ile Lys Arg Arg Tyr Thr Asn Pro Ile Gly						
	325		330			335
Arg Pro Lys Asn Arg Leu Lys Lys Gln Asn Thr Val Ser Lys Gly Pro						
	340		345			350
Phe Ser Lys Val Arg Thr Gly Pro Gly Arg Gly Arg Lys Arg Lys Ile						
	355		360			365
Thr Leu Ser Ser Gln Ser Ala Ser Ser Ser Ser Glu Glu Gly Tyr Leu						
	370		375			380
Glu Arg Ile Asp Gly Leu Asp Phe Cys Arg Asp Ser Asn Val Ser Leu						
	385		390			395
Arg Phe Asn Lys Lys Thr Lys Gly Leu Ile Asp Gly Leu Thr Lys Phe						
	405		410			415
Phe Thr Pro Ser Pro Asp Gly Arg Lys Ala Arg Gly Glu Val Val Asp						
	420		425			430
Tyr Ser Glu Gln Tyr Arg Ile Arg Lys Arg Gly Asn Arg Lys Ser Ser						
	435		440			445
Thr Ser Asp Trp Pro Thr Asp Asn Gln Asp Gly Trp Asp Gly Lys Gln						
	450		455			460

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Glu	Asn	Glu	Glu	Arg	Leu	Phe	Gly	Ser	Gln	Glu	Ile	Met	Thr	Glu	Lys	465	470	475	480
Asp	Met	Glu	Leu	Phe	Arg	Asp	Ile	Gln	Glu	Gln	Ala	Leu	Gln	Lys	Val	485	490	495	
Gly	Val	Thr	Gly	Pro	Pro	Asp	Pro	Gln	Val	Arg	Cys	Pro	Ser	Val	Ile	500	505	510	
Glu	Phe	Gly	Lys	Tyr	Glu	Ile	His	Thr	Trp	Tyr	Ser	Ser	Pro	Tyr	Pro	515	520	525	
Gln	Glu	Tyr	Ser	Arg	Leu	Pro	Lys	Leu	Tyr	Leu	Cys	Glu	Phe	Cys	Leu	530	535	540	
Lys	Tyr	Met	Lys	Ser	Arg	Thr	Ile	Leu	Gln	Gln	His	Met	Lys	Lys	Cys	545	550	555	560
Gly	Trp	Phe	His	Pro	Pro	Ala	Asn	Glu	Ile	Tyr	Arg	Lys	Asn	Asn	Ile	565	570	575	
Ser	Val	Phe	Glu	Val	Asp	Gly	Asn	Val	Ser	Thr	Ile	Tyr	Cys	Gln	Asn	580	585	590	
Leu	Cys	Leu	Leu	Ala	Lys	Leu	Phe	Leu	Asp	His	Lys	Thr	Leu	Tyr	Tyr	595	600	605	
Asp	Val	Glu	Pro	Phe	Leu	Phe	Tyr	Val	Leu	Thr	Gln	Asn	Asp	Val	Lys	610	615	620	
Gly	Cys	His	Leu	Val	Gly	Tyr	Phe	Ser	Lys	Glu	Lys	His	Cys	Gln	Gln	625	630	635	640
Lys	Tyr	Asn	Val	Ser	Cys	Ile	Met	Ile	Leu	Pro	Gln	Tyr	Gln	Arg	Lys	645	650	655	
Gly	Tyr	Gly	Arg	Phe	Leu	Ile	Asp	Phe	Ser	Tyr	Leu	Leu	Ser	Lys	Arg	660	665	670	
Glu	Gly	Gln	Ala	Gly	Ser	Pro	Glu	Lys	Pro	Leu	Ser	Asp	Leu	Gly	Arg	675	680	685	
Leu	Ser	Tyr	Met	Ala	Tyr	Trp	Lys	Ser	Val	Ile	Leu	Glu	Cys	Leu	Tyr	690	695	700	
His	Gln	Asn	Asp	Lys	Gln	Ile	Ser	Ile	Lys	Lys	Leu	Ser	Lys	Leu	Thr	705	710	715	720
Gly	Ile	Cys	Pro	Gln	Asp	Ile	Thr	Ser	Thr	Leu	His	His	Leu	Arg	Met	725	730	735	
Leu	Asp	Phe	Arg	Ser	Asp	Gln	Phe	Val	Ile	Ile	Arg	Arg	Glu	Lys	Leu	740	745	750	
Ile	Gln	Asp	His	Met	Ala	Lys	Leu	Gln	Leu	Asn	Leu	Arg	Pro	Val	Asp	755	760	765	

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Val	Asp	Pro	Glu	Cys	Leu	Arg	Trp	Thr	Pro	Val	Ile	Val	Ser	Asn	Ser	770	775	780
Val	Val	Ser	Glu	Glu	Glu	Glu	Glu	Glu	Ala	Glu	Glu	Gly	Glu	Asn	Glu	785	790	795
Glu	Pro	Gln	Cys	Gln	Glu	Arg	Glu	Leu	Glu	Ile	Ser	Val	Gly	Lys	Ser	805	810	815
Val	Ser	His	Glu	Asn	Lys	Glu	Gln	Asp	Ser	Tyr	Ser	Val	Glu	Ser	Glu	820	825	830
Lys	Lys	Pro	Glu	Val	Met	Ala	Pro	Val	Ser	Ser	Thr	Arg	Leu	Ser	Lys	835	840	845
Gln	Val	Leu	Pro	His	Asp	Ser	Leu	Pro	Ala	Asn	Ser	Gln	Pro	Ser	Arg	850	855	860
Arg	Gly	Arg	Trp	Gly	Arg	Lys	Asn	Arg	Lys	Thr	Gln	Glu	Arg	Phe	Gly	865	870	875
Asp	Lys	Asp	Ser	Lys	Leu	Leu	Leu	Glu	Glu	Thr	Ser	Ser	Ala	Pro	Gln	885	890	895
Glu	Gln	Tyr	Gly	Glu	Cys	Gly	Glu	Lys	Ser	Glu	Ala	Thr	Gln	Glu	Gln	900	905	910
Tyr	Thr	Glu	Ser	Glu	Glu	Gln	Leu	Val	Ala	Ser	Glu	Glu	Gln	Pro	Ser	915	920	925
Gln	Asp	Gly	Lys	Pro	Asp	Leu	Pro	Lys	Arg	Arg	Leu	Ser	Glu	Gly	Val	930	935	940
Glu	Pro	Trp	Arg	Gly	Gln	Leu	Lys	Lys	Ser	Pro	Glu	Ala	Leu	Lys	Cys	945	950	955
Arg	Leu	Thr	Glu	Gly	Ser	Glu	Arg	Leu	Pro	Arg	Arg	Tyr	Ser	Glu	Gly	965	970	975
Asp	Arg	Ala	Val	Leu	Arg	Gly	Phe	Ser	Glu	Ser	Ser	Glu	Glu	Glu	Glu	980	985	990
Glu	Pro	Glu	Ser	Pro	Arg	Ser	Ser	Ser	Pro	Pro	Ile	Leu	Thr	Lys	Pro	995	1000	1005
Thr	Leu	Lys	Arg	Lys	Lys	Pro	Phe	Leu	His	Arg	Arg	Arg	Arg	Val	Arg	1010	1015	1020
Lys	Arg	Lys	His	His	Asn	Ser	Ser	Val	Val	Thr	Glu	Thr	Ile	Ser	Glu	1025	1030	1035
Thr	Thr	Glu	Val	Leu	Asp	Glu	Pro	Phe	Glu	Asp	Ser	Asp	Ser	Glu	Arg	1045	1050	1055
Pro	Met	Pro	Arg	Leu	Glu	Pro	Thr	Phe	Glu	Ile	Asp	Glu	Glu	Glu	Glu	1060	1065	1070
Glu	Glu	Asp	Glu	Asn	Glu	Leu	Phe	Pro	Arg	Glu	Tyr	Phe	Arg	Arg	Leu			

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1075	1080	1085
Ser Ser Gln Asp Val Leu Arg Cys Gln Ser Ser Ser Lys Arg Lys Ser 1090	1095	1100
Lys Asp Glu Glu Glu Asp Glu Glu Ser Asp Asp Ala Asp Asp Thr Pro 1105	1110	1115 1120
Ile Leu Lys Pro Val Ser Leu Leu Arg Lys Arg Asp Val Lys Asn Ser 1125	1130	1135
Pro Leu Glu Pro Asp Thr Ser Thr Pro Leu Lys Lys Lys Lys Gly Trp 1140	1145	1150
Pro Lys Gly Lys Ser Arg Lys Pro Ile His Trp Lys Lys Arg Pro Gly 1155	1160	1165
Arg Lys Pro Gly Phe Lys Leu Ser Arg Glu Ile Met Pro Val Ser Thr 1170	1175	1180
Gln Ala Cys Val Ile Glu Pro Ile Val Ser Ile Pro Lys Ala Gly Arg 1185	1190	1195 1200
Lys Pro Lys Ile Gln Glu Ser Glu Glu Thr Val Glu Pro Lys Glu Asp 1205	1210	1215
Met Pro Leu Pro Glu Glu Arg Lys Glu Glu Glu Glu Met Gln Ala Glu 1220	1225	1230
Ala Glu Glu Ala Glu Glu Gly Glu Glu Glu Asp Ala Ala Ser Ser Glu 1235	1240	1245
Val Pro Ala Ala Ser Pro Ala Asp Ser Ser Asn Ser Pro Glu Thr Glu 1250	1255	1260
Thr Lys Glu Pro Glu Val Glu Glu Glu Glu Glu Lys Pro Arg Val Ser 1265	1270	1275 1280
Glu Glu Gln Arg Gln Ser Glu Glu Glu Gln Gln Glu Leu Glu Glu Pro 1285	1290	1295
Glu Pro Glu Glu Glu Glu Asp Ala Ala Ala Glu Thr Ala Gln Asn Asp 1300	1305	1310
Asp His Asp Ala Asp Asp Glu Asp Asp Gly His Leu Glu Ser Thr Lys 1315	1320	1325
Lys Lys Glu Leu Glu Glu Gln Pro Thr Arg Glu Asp Val Lys Glu Glu 1330	1335	1340
Pro Gly Val Gln Glu Ser Phe Leu Asp Ala Asn Met Gln Lys Ser Arg 1345	1350	1355 1360
Glu Lys Ile Lys Asp Lys Glu Glu Thr Glu Leu Asp Ser Glu Glu Glu 1365	1370	1375
Gln Pro Ser His Asp Thr Ser Val Val Ser Glu Gln Met Ala Gly Ser 1380	1385	1390

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Glu Asp Asp His Glu Glu Asp Ser His Thr Lys Glu Glu Leu Ile Glu
1395 1400 1405

Leu Lys Glu Glu Glu Glu Ile Pro His Ser Glu Leu Asp Leu Glu Thr
1410 1415 1420

Val Gln Ala Val Gln Ser Leu Thr Gln Glu Glu Ser Ser Glu His Glu
1425 1430 1435 1440

Gly Ala Tyr Gln Asp Cys Glu Glu Thr Leu Ala Ala Cys Gln Thr Leu
1445 1450 1455

Gln Ser Tyr Thr Gln Ala Asp Glu Asp Pro Gln Met Ser Met Val Glu
1460 1465 1470

Asp Cys His Ala Ser Glu His Asn Ser Pro Ile Ser Ser Val Gln Ser
1475 1480 1485

His Pro Ser Gln Ser Val Arg Ser Val Ser Ser Pro Asn Val Pro Ala
1490 1495 1500

Leu Glu Ser Gly Tyr Thr Gln Ile Ser Pro Glu Gln Gly Ser Leu Ser
1505 1510 1515 1520

Ala Pro Ser Met Gln Asn Met Glu Thr Ser Pro Met Met Asp Val Pro
1525 1530 1535

Ser Val Ser Asp His Ser Gln Gln Val Val Asp Ser Gly Phe Ser Asp
1540 1545 1550

Leu Gly Ser Ile Glu Ser Thr Thr Glu Asn Tyr Glu Asn Pro Ser Ser
1555 1560 1565

Tyr Asp Ser Thr Met Gly Gly Ser Ile Cys Gly Asn Ser Ser Ser Gln
1570 1575 1580

Ser Ser Cys Ser Tyr Gly Gly Leu Ser Ser Ser Ser Ser Leu Thr Gln
1585 1590 1595 1600

Ser Ser Cys Val Val Thr Gln Gln Met Ala Ser Met Gly Ser Ser Cys
1605 1610 1615

Ser Met Met Gln Gln Ser Ser Val Gln Pro Ala Ala Asn Cys Ser Ile
1620 1625 1630

Lys Ser Pro Gln Ser Cys Val Val Glu Arg Pro Pro Ser Asn Gln Gln
1635 1640 1645

Gln Gln Pro Pro Pro Pro Pro Pro Gln Gln Pro Gln Pro Pro Pro Pro
1650 1655 1660

Gln Pro Gln Pro Ala Pro Gln Pro Pro Pro Pro Gln Gln Gln Pro Gln
1665 1670 1675 1680

Gln Gln Pro Gln Pro Gln Pro Gln Gln Pro Pro Pro Pro Pro Pro Pro
1685 1690 1695

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Gln Gln Gln Pro Pro Leu Ser Gln Cys Ser Met Asn Asn Ser Phe Thr
 1700 1705 1710
 Pro Ala Pro Met Ile Met Glu Ile Pro Glu Ser Gly Ser Thr Gly Asn
 1715 1720 1725
 Ile Ser Ile Tyr Glu Arg Ile Pro Gly Asp Phe Gly Ala Gly Ser Tyr
 1730 1735 1740
 Ser Gln Pro Ser Ala Thr Phe Ser Leu Ala Lys Leu Gln Gln Leu Thr
 1745 1750 1755 1760
 Asn Thr Ile Met Asp Pro His Ala Met Pro Tyr Ser His Ser Pro Ala
 1765 1770 1775
 Val Thr Ser Tyr Ala Thr Ser Val Ser Leu Ser Asn Thr Gly Leu Ala
 1780 1785 1790
 Gln Leu Ala Pro Ser His Pro Leu Ala Gly Thr Pro Gln Ala Gln Ala
 1795 1800 1805
 Thr Met Thr Pro Pro Pro Asn Leu Ala Ser Thr Thr Met Asn Leu Thr
 1810 1815 1820
 Ser Pro Leu Leu Gln Cys Asn Met Ser Ala Thr Asn Ile Gly Ile Pro
 1825 1830 1835 1840
 His Thr Gln Arg Leu Gln Gly Gln Met Pro Val Lys Gly His Ile Ser
 1845 1850 1855
 Ile Arg Ser Lys Ser Ala Pro Leu Pro Ser Ala Ala Ala His Gln Gln
 1860 1865 1870
 Gln Leu Tyr Gly Arg Ser Pro Ser Ala Val Ala Met Gln Ala Gly Pro
 1875 1880 1885
 Arg Ala Leu Ala Val Gln Arg Gly Met Asn Met Gly Val Asn Leu Met
 1890 1895 1900
 Pro Thr Pro Ala Tyr Asn Val Asn Ser Met Asn Met Asn Thr Leu Asn
 1905 1910 1915 1920
 Ala Met Asn Ser Tyr Arg Met Thr Gln Pro Met Met Asn Ser Ser Tyr
 1925 1930 1935
 His Ser Asn Pro Ala Tyr Met Asn Gln Thr Ala Gln Tyr Pro Met Gln
 1940 1945 1950
 Met Gln Met Gly Met Met Gly Ser Gln Ala Tyr Thr Gln Gln Pro Met
 1955 1960 1965
 Gln Pro Asn Pro His Gly Asn Met Met Tyr Thr Gly Pro Ser His His
 1970 1975 1980
 Ser Tyr Met Asn Ala Ala Gly Val Pro Lys Gln Ser Leu Asn Gly Pro
 1985 1990 1995 2000
 Tyr Met Arg Arg

<210> 251
<211> 7869
<212> DNA
<213> Homo sapiens

<400> 251

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ttcttacaac	tttatgacga	gacccatgtg	tggtgctatt	gagaaattca	ttgggaagtt	180
ggaagacatt	tcaaacaca	ggttggtttg	gtttctatag	tacaattggg	gtggcattct	240
gttttgtgaa	aggaggaagg	acttaggcca	gaaaaactcat	atgctatggg	taactgggtc	300
ccagcctccg	agaatcctgt	tttccatggg	gtaaaaactta	ctcagcatca	ggataaggga	360
taacgactct	atggatatac	agaatccttc	accatggtaa	aactcgcaaa	cccgctttat	420
actgagtggg	ttttggaggc	catcaaaaaa	gtgaaaaagc	agaaacagcg	tccttcagaa	480
gaaaggatat	gcaatgctgt	gtcttcatcc	catggcttgg	atcgtaaaac	tgtttttagaa	540
caattggagt	tgagtgttaa	agatggaaca	atttttaaag	tctcaaataa	aggactcaat	600
tcctataaag	atcctgataa	tcctgggcca	atagcacttc	ctaagcctcg	gaacccatgga	660
aaattggata	ataaacaaaa	tgtggattgg	aataaactga	taaagcgggc	agttgagggc	720
ttggcagagt	ctgggtggctc	aactttgaaa	agcattgaac	gttttttgaa	aggtcagaag	780
gatgtgtctg	cattattcgg	aggcagtgtc	gcctctggct	ttcaccagca	gttacgattg	840
gctatcaaac	gtgccattgg	ccacggcaga	ctccttaaag	atggacctct	ttatcggtc	900
aacactaaag	caaccaacgt	ggatgggaaa	gagagtgtgt	agtctctttc	ctgtttacct	960
ccagtgtccc	ttcttcaca	tgaaaaggat	aagccggttg	ctgaaccaat	ccccatctgt	1020
agtttctgtc	ttggtacaaa	agaacaaaac	cgagaaaaga	agccagagga	actcatctcc	1080
tgtgccgact	gtggcaacag	tggccatcca	tcctgtttaa	agttttcccc	tgaactaacg	1140
gttcgagtga	aggccttacg	gtggcagtgc	atcgagtgtg	aaacatgcag	ctcctgtcga	1200
gatcaaggca	aaaatgcgga	taacatgctc	ttttgtgatt	catgtgaccg	aggttttcac	1260
atggagtgtt	gtgatccgcc	actcaccgtg	atgccaaaag	gcatgtggat	atgtcaaata	1320
tgctgcacct	ggaaaaaagg	acgaaaactt	ctacaaaaga	aggcagcaca	gataaaacgg	1380
cgctatacta	atccaatagg	acgtccaaaa	aacagggttaa	agaaacaaaa	cacggtatca	1440
aaaggtccct	tcagcaaagt	tcgaactggc	cctggaaggg	gtaggaaacg	aaaaatcact	1500
ctttccagcc	aatcagcatc	atcatcatca	gaagaaggat	atttagagcg	gatagatggc	1560
ttggacttct	gcagagatag	caatgtctcc	ttgagggtca	acaagaaaac	caaagggctc	1620
attgatggcc	ttaccaaat	ttttaccct	tcctctgatg	ggcggaaaagc	tcggggggaa	1680
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<211> 2442

<212> PRT

<213> Homo sapiens

<400> 252

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Leu Phe Asp Leu Glu Asn Asp Leu Pro Asp Glu Leu Ile Pro Asn Gly
          35                     40                     45

Gly Glu Leu Gly Leu Leu Asn Ser Gly Asn Leu Val Pro Asp Ala Ala
          50                     55                     60

Ser Lys His Lys Gln Leu Ser Glu Leu Leu Arg Gly Gly Ser Gly Ser
          65                     70                     75                     80

Ser Ile Asn Pro Gly Ile Gly Asn Val Ser Ala Ser Ser Pro Val Gln
          85                     90                     95

Gln Gly Leu Gly Gly Gln Ala Gln Gly Gln Pro Asn Ser Ala Asn Met
          100                    105                    110

Ala Ser Leu Ser Ala Met Gly Lys Ser Pro Leu Ser Gln Gly Asp Ser
          115                    120                    125

Ser Ala Pro Ser Leu Pro Lys Gln Ala Ala Ser Thr Ser Gly Pro Thr
          130                    135                    140

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 145 150 155 160
 Leu Ala Thr Ser Ser Pro Ala Thr Ser Gln Thr Gly Pro Gly Ile Cys
 165 170 175
 Met Asn Ala Asn Phe Asn Gln Thr His Pro Gly Leu Leu Asn Ser Asn
 180 185 190
 Ser Gly His Ser Leu Ile Asn Gln Ala Ser Gln Gly Gln Ala Gln Val
 195 200 205
 Met Asn Gly Ser Leu Gly Ala Ala Gly Arg Gly Arg Gly Ala Gly Met
 210 215 220
 Pro Tyr Pro Thr Pro Ala Met Gln Gly Ala Ser Ser Ser Val Leu Ala
 225 230 235 240
 Glu Thr Leu Thr Gln Val Ser Pro Gln Met Thr Gly His Ala Gly Leu
 245 250 255
 Asn Thr Ala Gln Ala Gly Gly Met Ala Lys Met Gly Ile Thr Gly Asn
 260 265 270
 Thr Ser Pro Phe Gly Gln Pro Phe Ser Gln Ala Gly Gly Gln Pro Met
 275 280 285
 Gly Ala Thr Gly Val Asn Pro Gln Leu Ala Ser Lys Gln Ser Met Val
 290 295 300
 Asn Ser Leu Pro Thr Phe Pro Thr Asp Ile Lys Asn Thr Ser Val Thr
 305 310 315 320
 Asn Val Pro Asn Met Ser Gln Met Gln Thr Ser Val Gly Ile Val Pro
 325 330 335
 Thr Gln Ala Ile Ala Thr Gly Pro Thr Ala Asp Pro Glu Lys Arg Lys
 340 345 350
 Leu Ile Gln Gln Gln Leu Val Leu Leu Leu His Ala His Lys Cys Gln
 355 360 365
 Arg Arg Glu Gln Ala Asn Gly Glu Val Arg Ala Cys Ser Leu Pro His
 370 375 380
 Cys Arg Thr Met Lys Asn Val Leu Asn His Met Thr His Cys Gln Ala
 385 390 395 400
 Gly Lys Ala Cys Gln Val Ala His Cys Ala Ser Ser Arg Gln Ile Ile
 405 410 415
 Ser His Trp Lys Asn Cys Thr Arg His Asp Cys Pro Val Cys Leu Pro
 420 425 430
 Leu Lys Asn Ala Ser Asp Lys Arg Asn Gln Gln Thr Ile Leu Gly Ser
 435 440 445

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Pro Ala Ser Gly Ile Gln Asn Thr Ile Gly Ser Val Gly Thr Gly Gln
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 Met Gln Arg Ala Tyr Ala Ala Leu Gly Leu Pro Tyr Met Asn Gln Pro
 485 490 495
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 Gln Thr His Gln Gln Met Arg Thr Leu Asn Pro Leu Gly Asn Asn Pro
 515 520 525
 Met Asn Ile Pro Ala Gly Gly Ile Thr Thr Asp Gln Gln Pro Pro Asn
 530 535 540
 Leu Ile Ser Glu Ser Ala Leu Pro Thr Ser Leu Gly Ala Thr Asn Pro
 545 550 555 560
 Leu Met Asn Asp Gly Ser Asn Ser Gly Asn Ile Gly Thr Leu Ser Thr
 565 570 575
 Ile Pro Thr Ala Ala Pro Pro Ser Ser Thr Gly Val Arg Lys Gly Trp
 580 585 590
 His Glu His Val Thr Gln Asp Leu Arg Ser His Leu Val His Lys Leu
 595 600 605
 Val Gln Ala Ile Phe Pro Thr Pro Asp Pro Ala Ala Leu Lys Asp Arg
 610 615 620
 Arg Met Glu Asn Leu Val Ala Tyr Ala Lys Lys Val Glu Gly Asp Met
 625 630 635 640
 Tyr Glu Ser Ala Asn Ser Arg Asp Glu Tyr Tyr His Leu Leu Ala Glu
 645 650 655
 Lys Ile Tyr Lys Ile Gln Lys Glu Leu Glu Glu Lys Arg Arg Ser Arg
 660 665 670
 Leu His Lys Gln Gly Ile Leu Gly Asn Gln Pro Ala Leu Pro Ala Pro
 675 680 685
 Gly Ala Gln Pro Pro Val Ile Pro Gln Ala Gln Pro Val Arg Pro Pro
 690 695 700
 Asn Gly Pro Leu Ser Leu Pro Val Asn Arg Met Gln Val Ser Gln Gly
 705 710 715 720
 Met Asn Ser Phe Asn Pro Met Ser Leu Gly Asn Val Gln Leu Pro Gln
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 Ala Pro Met Gly Pro Arg Ala Ala Ser Pro Met Asn His Ser Val Gln
 740 745 750
 Met Asn Ser Met Gly Ser Val Pro Gly Met Ala Ile Ser Pro Ser Arg

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770						775					780				
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785					790					795					800
Ser	Ser	Ser	Gly	Ala	Met	Ser	Val	Gly	Met	Gly	Gln	Pro	Pro	Ala	Gln
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Thr	Gly	Val	Ser	Gln	Gly	Gln	Val	Pro	Gly	Ala	Ala	Leu	Pro	Asn	Pro
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Leu	Asn	Met	Leu	Gly	Pro	Gln	Ala	Ser	Gln	Leu	Pro	Cys	Pro	Pro	Val
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Thr	Gln	Ser	Pro	Leu	His	Pro	Thr	Pro	Pro	Pro	Ala	Ser	Thr	Ala	Ala
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Gly	Met	Pro	Ser	Leu	Gln	His	Thr	Thr	Pro	Pro	Gly	Met	Thr	Pro	Pro
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Gln	Pro	Ala	Ala	Pro	Thr	Gln	Pro	Ser	Thr	Pro	Val	Ser	Ser	Ser	Gly
				885					890					895	
Gln	Thr	Pro	Thr	Pro	Thr	Pro	Gly	Ser	Val	Pro	Ser	Ala	Thr	Gln	Thr
			900					905					910		
Gln	Ser	Thr	Pro	Thr	Val	Gln	Ala	Ala	Ala	Gln	Ala	Gln	Val	Thr	Pro
		915					920					925			
Gln	Pro	Gln	Thr	Pro	Val	Gln	Pro	Pro	Ser	Val	Ala	Thr	Pro	Gln	Ser
		930				935					940				
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Leu	Ser	Gln	Ala	Ala	Ala	Ser	Ile	Asp	Asn	Arg	Val	Pro	Thr	Pro	Ser
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Ser	Val	Ala	Ser	Ala	Glu	Thr	Asn	Ser	Gln	Gln	Pro	Gly	Pro	Asp	Val
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Pro	Val	Leu	Glu	Met	Lys	Thr	Glu	Thr	Gln	Ala	Glu	Asp	Thr	Glu	Pro
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Gln	Lys	Ser	Glu	Pro	Met	Glu	Val	Asp	Glu	Lys	Lys	Pro	Glu	Val	Lys
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Val	Glu	Val	Lys	Glu	Glu	Glu	Glu	Ser	Ser	Ser	Asn	Gly	Thr	Ala	Ser
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Gln Ser Thr Ser Pro Ser Gln Pro Arg Lys Lys Ile Phe Lys Pro Glu
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Glu Leu Arg Gln Ala Leu Met Pro Thr Leu Glu Ala Leu Tyr Arg Gln
 1090 1095 1100

Asp Pro Glu Ser Leu Pro Phe Arg Gln Pro Val Asp Pro Gln Leu Leu
 1105 1110 1115 1120

Gly Ile Pro Asp Tyr Phe Asp Ile Val Lys Asn Pro Met Asp Leu Ser
 1125 1130 1135

Thr Ile Lys Arg Lys Leu Asp Thr Gly Gln Tyr Gln Glu Pro Trp Gln
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Tyr Val Asp Asp Val Trp Leu Met Phe Asn Asn Ala Trp Leu Tyr Asn
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Arg Lys Thr Ser Arg Val Tyr Lys Phe Cys Ser Lys Leu Ala Glu Val
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Phe Glu Gln Glu Ile Asp Pro Val Met Gln Ser Leu Gly Tyr Cys Cys
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Gly Arg Lys Tyr Glu Phe Ser Pro Gln Thr Leu Cys Cys Tyr Gly Lys
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Gln Leu Cys Thr Ile Pro Arg Asp Ala Ala Tyr Tyr Ser Tyr Gln Asn
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Arg Tyr His Phe Cys Glu Lys Cys Phe Thr Glu Ile Gln Gly Glu Asn
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Val Thr Leu Gly Asp Asp Pro Ser Gln Pro Gln Thr Thr Ile Ser Lys
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Asp Gln Phe Glu Lys Lys Lys Asn Asp Thr Leu Asp Pro Glu Pro Phe
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Val Asp Cys Lys Glu Cys Gly Arg Lys Met His Gln Ile Cys Val Leu
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His Tyr Asp Ile Ile Trp Pro Ser Gly Phe Val Cys Asp Asn Cys Leu
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Lys Lys Thr Gly Arg Pro Arg Lys Glu Asn Lys Phe Ser Ala Lys Arg
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Leu Gln Thr Thr Arg Leu Gly Asn His Leu Glu Asp Arg Val Asn Lys
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Phe Leu Arg Arg Gln Asn His Pro Glu Ala Gly Glu Val Phe Val Arg
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Val Val Ala Ser Ser Asp Lys Thr Val Glu Val Lys Pro Gly Met Lys
 1365 1370 1375

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Ser Arg Phe Val Asp Ser Gly Glu Met Ser Glu Ser Phe Pro Tyr Arg
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 1460 1465 1470
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 1490 1495 1500
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 1635 1640 1645
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 1665 1670 1675 1680
 Leu Arg Arg Ser Lys Trp Ser Thr Leu Cys Met Leu Val Glu Leu His

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1685	1690	1695
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Cys Ile Asn Cys Tyr Asn Thr Lys Ser His Ala His Lys Met Val Lys 1730	1735	1740
Trp Gly Leu Gly Leu Asp Asp Glu Gly Ser Ser Gln Gly Glu Pro Gln 1745	1750	1755 1760
Ser Lys Ser Pro Gln Glu Ser Arg Arg Leu Ser Ile Gln Arg Cys Ile 1765	1770	1775
Gln Ser Leu Val His Ala Cys Gln Cys Arg Asn Ala Asn Cys Ser Leu 1780	1785	1790
Pro Ser Cys Gln Lys Met Lys Arg Val Val Gln His Thr Lys Gly Cys 1795	1800	1805
Lys Arg Lys Thr Asn Gly Gly Cys Pro Val Cys Lys Gln Leu Ile Ala 1810	1815	1820
Leu Cys Cys Tyr His Ala Lys His Cys Gln Glu Asn Lys Cys Pro Val 1825	1830	1835 1840
Pro Phe Cys Leu Asn Ile Lys His Lys Leu Arg Gln Gln Gln Ile Gln 1845	1850	1855
His Arg Leu Gln Gln Ala Gln Leu Met Arg Arg Arg Met Ala Thr Met 1860	1865	1870
Asn Thr Arg Asn Val Pro Gln Gln Ser Leu Pro Ser Pro Thr Ser Ala 1875	1880	1885
Pro Pro Gly Thr Pro Thr Gln Gln Pro Ser Thr Pro Gln Thr Pro Gln 1890	1895	1900
Pro Pro Ala Gln Pro Gln Pro Ser Pro Val Ser Met Ser Pro Ala Gly 1905	1910	1915 1920
Phe Pro Ser Val Ala Arg Thr Gln Pro Pro Thr Thr Val Ser Thr Gly 1925	1930	1935
Lys Pro Thr Ser Gln Val Pro Ala Pro Pro Pro Pro Ala Gln Pro Pro 1940	1945	1950
Pro Ala Ala Val Glu Ala Ala Arg Gln Ile Glu Arg Glu Ala Gln Gln 1955	1960	1965
Gln Gln His Leu Tyr Arg Val Asn Ile Asn Asn Ser Met Pro Pro Gly 1970	1975	1980
Arg Thr Gly Met Gly Thr Pro Gly Ser Gln Met Ala Pro Val Ser Leu 1985	1990	1995 2000

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Leu Ser Gly Gln Pro Gln Ala Ser His Leu Pro Gly Gln Gln Ile Ala
 2325 2330 2335

Thr Ser Leu Ser Asn Gln Val Arg Ser Pro Ala Pro Val Gln Ser Pro
 2340 2345 2350

Arg Pro Gln Ser Gln Pro Pro His Ser Ser Pro Ser Pro Arg Ile Gln
 2355 2360 2365

Pro Gln Pro Ser Pro His His Val Ser Pro Gln Thr Gly Ser Pro His
 2370 2375 2380

Pro Gly Leu Ala Val Thr Met Ala Ser Ser Ile Asp Gln Gly His Leu
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Gly Asn Pro Glu Gln Ser Ala Met Leu Pro Gln Leu Asn Thr Pro Ser
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<212> DNA

<213> Homo sapiens

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<212> PRT

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 atttttacta gtttgcccg gccaagccag tgttgaacta ctggcctcaa gtgatcctcc 420
 caccttggcc tccccaaagt gcatccctac aggcattgagc cactgcactc agcctgaact 480
 ttcgaaattt attttaagg cccactttta aatgcttctt ttcagcagct aactttccag 540
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 gctt 604

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<400> 258
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 1 5 10 15

<210> 259
 <211> 45
 <212> DNA
 <213> Homo sapiens

<400> 259
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<210> 260
<211> 15
<212> PRT
<213> Homo sapiens

<400> 260
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1 5 10 15

<210> 261
<211> 45
<212> DNA
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<400> 261
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<210> 262
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<210> 263
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<210> 264
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<213> Homo sapiens

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Gln Asn Pro Asn Ser Lys Glu Gly Leu Gln Pro Ile Tyr Trp Ser
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<210> 265
<211> 45
<212> DNA
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212/299

<210> 266

<211> 829

<212> PRT

<213> Homo sapiens

<400> 266

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Val Glu Leu Asn Lys Arg Leu Gln Gln Thr Glu Arg Glu Arg Asp Leu
 35 40 45

Leu Glu Lys Lys Leu Ala Lys Ala Gln Cys Glu Gln Ser His Leu Met
 50 55 60

Arg Glu His Glu Asp Val Gln Glu Arg Thr Thr Leu Arg Tyr Glu Glu
 65 70 75 80

Arg Ile Thr Glu Leu His Ser Val Ile Ala Glu Leu Asn Lys Lys Ile
 85 90 95

Asp Arg Leu Gln Gly Thr Thr Ile Arg Glu Glu Asp Glu Tyr Ser Glu
 100 105 110

Leu Arg Ser Glu Leu Ser Gln Ser Gln His Glu Val Asn Glu Asp Ser
 115 120 125

Arg Ser Met Asp Gln Asp Gln Thr Ser Val Ser Ile Pro Glu Asn Gln
 130 135 140

Ser Thr Met Val Thr Ala Asp Met Asp Asn Cys Ser Asp Leu Asn Ser
 145 150 155 160

Glu Leu Gln Arg Val Leu Thr Gly Leu Glu Asn Val Val Cys Gly Arg
 165 170 175

Lys Lys Ser Ser Cys Ser Leu Ser Val Ala Glu Val Asp Arg His Ile
 180 185 190

Glu Gln Leu Thr Thr Ala Ser Glu His Cys Asp Leu Ala Ile Lys Thr
 195 200 205

Val Glu Glu Ile Glu Gly Val Leu Gly Arg Asp Leu Tyr Pro Asn Leu
 210 215 220

Ala Glu Glu Arg Ser Arg Trp Glu Lys Glu Leu Ala Gly Leu Arg Glu
 225 230 235 240

Glu Asn Glu Ser Leu Thr Ala Met Leu Cys Ser Lys Glu Glu Glu Leu
 245 250 255

Asn Arg Thr Lys Ala Thr Met Asn Ala Ile Arg Glu Glu Arg Asp Arg
 260 265 270

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Leu Arg Arg Arg Val Arg Glu Leu Gln Thr Arg Leu Gln Ser Val Gln
 275 280 285
 Ala Thr Gly Pro Ser Ser Pro Gly Arg Leu Thr Ser Thr Asn Arg Pro
 290 295 300
 Ile Asn Pro Ser Thr Gly Glu Leu Ser Thr Ser Ser Ser Ser Asn Asp
 305 310 315 320
 Ile Pro Ile Ala Lys Ile Ala Glu Arg Val Lys Leu Ser Lys Thr Arg
 325 330 335
 Ser Glu Ser Ser Ser Ser Asp Arg Pro Val Leu Gly Ser Glu Ile Ser
 340 345 350
 Ser Ile Gly Val Ser Ser Ser Val Ala Glu His Leu Ala His Ser Leu
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 Gln Asp Cys Ser Asn Ile Gln Glu Ile Phe Gln Thr Leu Tyr Ser His
 370 375 380
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 385 390 395 400
 Glu Arg Leu Asn Ser Arg Ile Glu His Leu Lys Ser Gln Asn Asp Leu
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 435 440 445
 Leu Gln Tyr Ser Glu Gln Cys Ile Glu Ala Tyr Glu Leu Leu Leu Ala
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 Leu Ala Glu Ser Glu Gln Ser Leu Ile Leu Gly Gln Phe Arg Ala Ala
 465 470 475 480
 Gly Val Gly Ser Ser Pro Gly Asp Gln Ser Gly Asp Glu Asn Ile Thr
 485 490 495
 Gln Met Leu Lys Arg Ala His Asp Cys Arg Lys Thr Ala Glu Asn Ala
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 Ala Lys Ala Leu Leu Met Lys Leu Asp Gly Ser Cys Gly Gly Ala Phe
 515 520 525
 Ala Val Ala Gly Cys Ser Val Gln Pro Trp Glu Ser Leu Ser Ser Asn
 530 535 540
 Ser His Thr Ser Thr Thr Ser Ser Thr Ala Ser Ser Cys Asp Thr Glu
 545 550 555 560
 Phe Thr Lys Glu Asp Glu Gln Arg Leu Lys Asp Tyr Ile Gln Gln Leu
 565 570 575
 Lys Asn Asp Arg Ala Ala Val Lys Leu Thr Met Leu Glu Leu Glu Ser

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580					585					590					
Ile	His	Ile	Asp	Pro	Leu	Ser	Tyr	Asp	Val	Lys	Pro	Arg	Gly	Asp	Ser
		595					600					605			
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	610					615					620				
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Lys	Glu	Lys	Lys	Ala	Leu	Glu	Leu	Lys	Leu	Ser	Thr	Arg	Glu	Ala	Gln
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705					710					715					720
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Val	Gln	Glu	Leu	Val	Ser	Ala	Leu	Glu	Arg	Leu	Thr	Lys	Ser	Ser	Glu
			740					745					750		
Ile	Arg	His	Gln	Gln	Ser	Ala	Glu	Phe	Val	Asn	Asp	Leu	Lys	Arg	Ala
		755					760					765			
Asn	Ser	Asn	Leu	Val	Ala	Ala	Tyr	Glu	Lys	Ala	Lys	Lys	Lys	His	Gln
	770					775					780				
Asn	Lys	Leu	Lys	Lys	Leu	Glu	Ser	Gln	Met	Met	Ala	Met	Val	Glu	Arg
785					790					795					800
His	Glu	Thr	Gln	Val	Arg	Met	Leu	Lys	Gln	Arg	Ile	Ala	Leu	Leu	Glu
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<210> 267

<211> 4181

<212> DNA

<213> Homo sapiens

<400> 267

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agacctgggg gactgagagc ccagctctga aaagtgcac atgaattccg gagttgccat 240

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<210> 268

<211> 1172

<212> DNA

<213> Homo sapiens

<400> 268

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<210> 269

<211> 318

<212> PRT

<213> Homo sapiens

<400> 269

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 20             25             30

Leu Lys Arg Glu Leu Gly Glu Gly Ala Phe Gly Lys Val Phe Leu Ala
 35             40             45

Glu Cys Tyr Asn Leu Ser Pro Thr Lys Asp Lys Met Leu Val Ala Val
 50             55             60

Lys Ala Leu Lys Asp Pro Thr Leu Ala Ala Arg Lys Asp Phe Gln Arg
 65             70             75             80
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Met	Lys	His	Gly	Asp	Leu	Asn	Lys	Phe	Leu	Arg	Ala	His	Gly	Pro	Asp	
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Ala	Met	Ile	Leu	Val	Asp	Gly	Gln	Pro	Arg	Gln	Ala	Lys	Gly	Glu	Leu	
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Gly	Leu	Ser	Gln	Met	Leu	His	Ile	Ala	Ser	Gln	Ile	Ala	Ser	Gly	Met	
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Val	Tyr	Leu	Ala	Ser	Gln	His	Phe	Val	His	Arg	Asp	Leu	Ala	Thr	Arg	
			165							170				175		
Asn	Cys	Leu	Val	Gly	Ala	Asn	Leu	Leu	Val	Lys	Ile	Gly	Asp	Phe	Gly	
			180							185				190		
Met	Ser	Arg	Asp	Val	Tyr	Ser	Thr	Asp	Tyr	Tyr	Arg	Val	Gly	Gly	His	
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Thr	Met	Leu	Pro	Ile	Arg	Trp	Met	Pro	Pro	Glu	Ser	Ile	Met	Tyr	Arg	
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Lys	Phe	Thr	Thr	Glu	Ser	Asp	Val	Trp	Ser	Phe	Gly	Val	Ile	Leu	Trp	
225					230					235					240	
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<210> 271

<211> 408

<212> PRT

<213> Homo sapiens

<400> 271

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      20              25              30

Pro Arg Gln Glu Ser Thr Arg Val Ile Gln Leu Met Pro Ser Pro Ile
      35              40              45

Met His Pro Leu Ile Leu Asn Pro Arg His Ser Val Asp Phe Lys Gln
      50              55              60

Ser Arg Leu Ser Glu Asp Gly Leu His Arg Glu Gly Lys Pro Ile Asn
      65              70              75              80

Leu Ser His Arg Glu Asp Leu Ala Tyr Met Asn His Ile Met Val Ser
      85              90              95

Val Ser Pro Pro Glu Glu His Ala Met Pro Ile Gly Arg Ile Ala Asp
      100              105              110

Val Gln His Ile Lys Arg Arg Asp Ile Val Leu Lys Arg Glu Leu Gly
      115              120              125

Glu Gly Ala Phe Gly Lys Val Phe Leu Ala Glu Cys Tyr Asn Leu Ser
      130              135              140

Pro Thr Lys Asp Lys Met Leu Val Ala Val Lys Ala Leu Lys Asp Pro
      145              150              155              160

Thr Leu Ala Ala Arg Lys Asp Phe Gln Arg Glu Ala Glu Leu Leu Thr
      165              170              175

Asn Leu Gln His Glu His Ile Val Lys Phe Tyr Gly Val Cys Gly Asp
      180              185              190

Gly Asp Pro Leu Ile Met Val Phe Glu Tyr Met Lys His Gly Asp Leu
      195              200              205

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Asn Lys Phe Leu Arg Ala His Gly Pro Asp Ala Met Ile Leu Val Asp
 210 215 220
 Gly Gln Pro Arg Gln Ala Lys Gly Glu Leu Gly Leu Ser Gln Met Leu
 225 230 235 240
 His Ile Ala Ser Gln Ile Ala Ser Gly Met Val Tyr Leu Ala Ser Gln
 245 250 255
 His Phe Val His Arg Asp Leu Ala Thr Arg Asn Cys Leu Val Gly Ala
 260 265 270
 Asn Leu Leu Val Lys Ile Gly Asp Phe Gly Met Ser Arg Asp Val Tyr
 275 280 285
 Ser Thr Asp Tyr Tyr Arg Val Gly Gly His Thr Met Leu Pro Ile Arg
 290 295 300
 Trp Met Pro Pro Glu Ser Ile Met Tyr Arg Lys Phe Thr Thr Glu Ser
 305 310 315 320
 Asp Val Trp Ser Phe Gly Val Ile Leu Trp Glu Ile Phe Thr Tyr Gly
 325 330 335
 Lys Gln Pro Trp Phe Gln Leu Ser Asn Thr Glu Val Ile Glu Cys Ile
 340 345 350
 Thr Gln Gly Arg Val Leu Glu Arg Pro Arg Val Cys Pro Lys Glu Val
 355 360 365
 Tyr Asp Val Met Leu Gly Cys Trp Gln Arg Glu Pro Gln Gln Arg Leu
 370 375 380
 Asn Ile Lys Glu Ile Tyr Lys Ile Leu His Ala Leu Gly Lys Ala Thr
 385 390 395 400
 Pro Ile Tyr Leu Asp Ile Leu Gly
 405

<210> 272

<211> 1403

<212> DNA

<213> Homo sapiens

<400> 272

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 ccagcgtcct ccgagtccca cccgaagcca tccagccccc ggcaggagag cacacgcgtg 120
 atccagctga tgcccagccc catcatgcac cctctgatcc tgaacccccg gcactccgtg 180
 gatttcaaac agtccaggct ctccgaggac gggctgcata ggggaaggga gcccatcaac 240
 ctctctcatc gggaagacct ggcttacatg aaccacatca tggctctctgt ctccccgcct 300
 gaagagcacg ccatgcccat tgggagaata gcagatgtgc agcacattaa gaggagagac 360
 atcgtgctga agcgagaact ggggtgaggga gcctttggaa aggtcttcct ggccgagtgc 420
 tacaacctca gcccgaccaa ggacaagatg cttgtggctg tgaaggccct gaaggatccc 480
 accctggctg cccggaagga tttccagagg gaggccgagc tgctcaccac cctgcagcat 540
 gagcacattg tcaagttcta tggagtgtgc ggcgatgggg accccctcat catggctctt 600
 gaatacatga agcatggaga cctgaataag ttccctcaggg cccatgggac agatgcaatg 660

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atccttgtgg atggacagcc acgccaggcc aaggggtgagc tggggctctc ccaaagtctc 720
cacattgcca gtcagatcgc ctcggttatg gtgtacctgg cctcccagca ctttgtgcac 780
cgagacctgg ccaccaggaa ctgcctggtt ggagcgaatc tgctagttaa gattggggac 840
ttcggcatgt ccagagatgt ctacagcacg gattattaca ggggtgggagg acacaccatg 900
ctcccattc gctggatgcc tcctgaaagc atcatgtacc ggaagttcac tacagagagt 960
gatgtatgga gcttcggggg gatcctctgg gagatcttca cctatggaaa gcagccatgg 1020
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ccccgagtct gcccacaaaga ggtgtacgat gtcattgctgg ggtgctggca gagggaaacca 1140
cagcagcggg tgaacatcaa ggagatctac aaaatcctcc atgctttggg gaaggccacc 1200
ccaatctacc tggacattct tggctagtgg tggctgggtg tcatgaattc atactctgtt 1260
gcctcctctc tccttgccct acatctccct tccacctcac aactccttcc atccttgact 1320
gaagcgaaca tcttcatata aactcaagtg cctgctacac atacaacact gaaaaaagga 1380
aaaaaaaaga aaaaaaaaaa aaa 1403

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<210> 273

<211> 536

<212> PRT

<213> Homo sapiens

<400> 273

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Met Gly Ser Asn Lys Ser Lys Pro Lys Asp Ala Ser Gln Arg Arg Arg
 1              5              10              15

Ser Leu Glu Pro Ala Glu Asn Val His Gly Ala Gly Gly Gly Ala Phe
          20              25              30

Pro Ala Ser Gln Thr Pro Ser Lys Pro Ala Ser Ala Asp Gly His Arg
          35              40              45

Gly Pro Ser Ala Ala Phe Ala Pro Ala Ala Ala Glu Pro Lys Leu Phe
          50              55              60

Gly Gly Phe Asn Ser Ser Asp Thr Val Thr Ser Pro Gln Arg Ala Gly
          65              70              75              80

Pro Leu Ala Gly Gly Val Thr Thr Phe Val Ala Leu Tyr Asp Tyr Glu
          85              90              95

Ser Arg Thr Glu Thr Asp Leu Ser Phe Lys Lys Gly Glu Arg Leu Gln
          100              105              110

Ile Val Asn Asn Thr Glu Gly Asp Trp Trp Leu Ala His Ser Leu Ser
          115              120              125

Thr Gly Gln Thr Gly Tyr Ile Pro Ser Asn Tyr Val Ala Pro Ser Asp
          130              135              140

Ser Ile Gln Ala Glu Glu Trp Tyr Phe Gly Lys Ile Thr Arg Arg Glu
          145              150              155              160

Ser Glu Arg Leu Leu Leu Asn Ala Glu Asn Pro Arg Gly Thr Phe Leu
          165              170              175

Val Arg Glu Ser Glu Thr Thr Lys Gly Ala Tyr Cys Leu Ser Val Ser
          180              185              190

Asp Phe Asp Asn Ala Lys Gly Leu Asn Val Lys His Tyr Lys Ile Arg

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195					200					205					
Lys	Leu	Asp	Ser	Gly	Gly	Phe	Tyr	Ile	Thr	Ser	Arg	Thr	Gln	Phe	Asn
210					215					220					
Ser	Leu	Gln	Gln	Leu	Val	Ala	Tyr	Tyr	Ser	Lys	His	Ala	Asp	Gly	Leu
225				230						235					240
Cys	His	Arg	Leu	Thr	Thr	Val	Cys	Pro	Thr	Ser	Lys	Pro	Gln	Thr	Gln
				245					250					255	
Gly	Leu	Ala	Lys	Asp	Ala	Trp	Glu	Ile	Pro	Arg	Glu	Ser	Leu	Arg	Leu
			260				265						270		
Glu	Val	Lys	Leu	Gly	Gln	Gly	Cys	Phe	Gly	Glu	Val	Trp	Met	Gly	Thr
		275					280					285			
Trp	Asn	Gly	Thr	Thr	Arg	Val	Ala	Ile	Lys	Thr	Leu	Lys	Pro	Gly	Thr
	290					295					300				
Met	Ser	Pro	Glu	Ala	Phe	Leu	Gln	Glu	Ala	Gln	Val	Met	Lys	Lys	Leu
305				310						315					320
Arg	His	Glu	Lys	Leu	Val	Gln	Leu	Tyr	Ala	Val	Val	Ser	Glu	Glu	Pro
				325					330					335	
Ile	Tyr	Ile	Val	Thr	Glu	Tyr	Met	Ser	Lys	Gly	Ser	Leu	Leu	Asp	Phe
			340					345					350		
Leu	Lys	Gly	Glu	Thr	Gly	Lys	Tyr	Leu	Arg	Leu	Pro	Gln	Leu	Val	Asp
		355					360					365			
Met	Ala	Ala	Gln	Ile	Ala	Ser	Gly	Met	Ala	Tyr	Val	Glu	Arg	Met	Asn
						375					380				
Tyr	Val	His	Arg	Asp	Leu	Arg	Ala	Ala	Asn	Ile	Leu	Val	Gly	Glu	Asn
385				390					395						400
Leu	Val	Cys	Lys	Val	Ala	Asp	Phe	Gly	Leu	Ala	Arg	Leu	Ile	Glu	Asp
				405					410					415	
Asn	Glu	Tyr	Thr	Ala	Arg	Gln	Gly	Ala	Lys	Phe	Pro	Ile	Lys	Trp	Thr
			420					425					430		
Ala	Pro	Glu	Ala	Ala	Leu	Tyr	Gly	Arg	Phe	Thr	Ile	Lys	Ser	Asp	Val
		435					440					445			
Trp	Ser	Phe	Gly	Ile	Leu	Leu	Thr	Glu	Leu	Thr	Thr	Lys	Gly	Arg	Val
						455					460				
Pro	Tyr	Pro	Gly	Met	Val	Asn	Arg	Glu	Val	Leu	Asp	Gln	Val	Glu	Arg
465				470						475					480
Gly	Tyr	Arg	Met	Pro	Cys	Pro	Pro	Glu	Cys	Pro	Glu	Ser	Leu	His	Asp
				485					490					495	
Leu	Met	Cys	Gln	Cys	Trp	Arg	Lys	Glu	Pro	Glu	Glu	Arg	Pro	Thr	Phe
			500					505					510		

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Glu Tyr Leu Gln Ala Phe Leu Glu Asp Tyr Phe Thr Ser Thr Glu Pro
 515 520 525

Gln Tyr Gln Pro Gly Glu Asn Leu
 530 535

<210> 274
 <211> 1611
 <212> DNA
 <213> Homo sapiens

<400> 274
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 ccagcctcgg ccgacggcca ccgcgggccc agcgcgccct tcgccccgcg ggccgcccag 180
 cccaagctgt tcggaggcct caactcctcg gacaccgtca cctccccgca gagggcgggc 240
 ccgctggccg gtggagtgcac cacctttgtg gccctctatg actatgagtc taggacggag 300
 acagacctgt ccttcaagaa aggcgagcgg ctccagattg tcaacaacac agaggggagac 360
 tgggtggctgg cccactcgct cagcacagga cagacaggct acatccccag caactacgtg 420
 gcgccctccg actccatcca ggctgaggag tggatatttg gcaagatcac cagacgggag 480
 tcagagcggg tactgctcaa tgcagagaac ccgagaggga ccttcctcgt gcgagaaaagt 540
 gagaccacga aaggtgccta ctgcctctca gtgtctgact tcgacaacgc caagggcctc 600
 aacgtgaagc actacaagat ccgcaagctg gacagcggcg gcttctacat cacctcccgc 660
 acccagttca acagcctgca gcagctgggt gcctactact ccaaacacgc cgatggcctg 720
 tgccaccgcc tcaccaccgt gtgccccacg tccaagccgc agactcaggg cctggccaag 780
 gatgcctggg agatccctcg ggagtcgctg cggctggagg tcaagctggg ccagggctgc 840
 tttggcgagg tgtggatggg gacctggaac ggtaccacca ggggtggccat caaaaccctg 900
 aagcctggca cgatgtctcc agaggccttc ctgcaggagg cccagggtcat gaagaagctg 960
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 ctgcggctgc ctgagctggt ggacatggct gctcagatcg cctcaggcat ggcgtacgtg 1140
 gagcggatga actacgtcca ccgggacctt cgtgcagcca acatcctggt gggagagaac 1200
 ctggtgtgca aagtggccga ctttgggctg gctcggctca ttgaagacaa tgagtacacg 1260
 gcgcggcaag gtgccaaatt ccccatcaag tggacggctc cagaagctgc cctctatggc 1320
 cgcttcacca tcaagtccga cgtgtgggtc ttccgggatcc tgctgactga gctcaccaca 1380
 aagggacggg tgccctaccc tgggatgggt aaccgcgagg tgctggacca ggtggagcgg 1440
 ggctaccgga tgccctgccc gccggagtgt cccgagtccc tgcacgacct catgtgccag 1500
 tgctggcgga aggagcctga ggagcggccc accttcagat acctgcaggc cttcctggag 1560
 gactacttca cgtccaccga gccccagtag cagcccgggg agaacctcta g 1611

<210> 275
 <211> 226
 <212> PRT
 <213> Homo sapiens

<400> 275
 Met Tyr His Ala Ser Lys Leu Ser Ile Asp Glu Glu Val Tyr Phe Glu
 1 5 10 15
 Asn Leu Met Gln Leu Val Glu His Tyr Thr Ser Asp Ala Asp Gly Leu
 20 25 30
 Cys Thr Arg Leu Ile Lys Pro Lys Val Met Glu Gly Thr Val Ala Ala
 35 40 45

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Gln Asp Glu Phe Tyr Arg Ser Gly Trp Ala Leu Asn Met Lys Glu Leu
 50 55 60
 Lys Leu Leu Gln Thr Ile Gly Lys Gly Glu Phe Gly Asp Val Met Leu
 65 70 75 80
 Gly Asp Tyr Arg Gly Asn Lys Val Ala Val Lys Cys Ile Lys Asn Asp
 85 90 95
 Ala Thr Ala Gln Ala Phe Leu Ala Glu Ala Ser Val Met Thr Gln Leu
 100 105 110
 Arg His Ser Asn Leu Val Gln Leu Leu Gly Val Ile Val Glu Glu Lys
 115 120 125
 Gly Gly Leu Tyr Ile Val Thr Glu Tyr Met Ala Lys Gly Ser Leu Val
 130 135 140
 Asp Tyr Leu Arg Ser Arg Gly Arg Ser Val Leu Gly Gly Asp Cys Leu
 145 150 155 160
 Leu Lys Phe Ser Leu Asp Val Cys Glu Ala Met Glu Tyr Leu Glu Gly
 165 170 175
 Asn Asn Phe Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Ser
 180 185 190
 Glu Asp Asn Val Ala Lys Val Ser Asp Phe Gly Leu Thr Lys Glu Ala
 195 200 205
 Ser Thr Pro Arg Thr Arg Ala Ser Cys Gln Ser Ser Gly Gln Pro Leu
 210 215 220
 Arg Pro
 225

<210> 276

<211> 2442

<212> DNA

<213> Homo sapiens

<400> 276

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 ctcccccttc tccccccgac tccctccctc ccccttcccc cgcctttctt cctctccgca 180
 ccggggcgt gcgtccgtcc cctgcctct gcttggcggt cctctctccc ctctccttgc 240
 acccatacct ctttgtaccg caccocctgg gtatccctgc gccctcccc tccccctga 300
 ccgcatggac cgtcccgag gccgctgatg ccgcccgcgg gacggtggcc cggaccgcag 360
 tgccccaaga gagctctaag ggtaccaagt gacaggttgg cttaactgag actcggggac 420
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 attgccaagt acaacttcca cggcactgcc gagcaggacc tgcccttctg caaaggagac 540
 gtgctcacca ttgtggccgt caccaaggac cccaactggg acaaagccaa aaacaagggtg 600
 ggccgtgagg gcatcatccc agccaactac gtccagaagc gggagggcgt gaaggcgggt 660
 accaaactca gcctcatgcc gtgagttcca cggcaagatc acacgggagc aggtgagcg 720
 gcttctgtac ccgcccggaga caggcctgtt cctggtgcgg gagagcacca actaccccg 780
 agactacacg ctgtgcgtga gctgcgacgg caaggtggag cactaccgca tcatgtacca 840
 tgccagcaag ctcagcatcg acgaggaggt gtactttgag aacctcatgc agctggtgga 900

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gcactacacc tcagacgcag atggactctg tacgcgcctc attaaaccaa aggtcatgga 960
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gctgaagctg ctgcagacca tcgggaaggg ggagttcggg gacgtgatgc tgggcgatta 1080
ccgaggggaac aaagtcgccc tcaagtgcac taagaacgac gccactgccc aggccttcct 1140
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gcgcccagag cagacgtctg tcaggggctt ggatttcgtg tgccgctgcc acccgcccac 2400
ccgccttgtg agatggaatt gtaataaacc acgcatgag ga 2442

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<210> 277

<211> 1114

<212> PRT

<213> Homo sapiens

<400> 277

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Met Ala Lys Ala Thr Ser Gly Ala Ala Gly Leu Arg Leu Leu Leu Leu
  1                      5                      10                      15

Leu Leu Leu Pro Leu Leu Gly Lys Val Ala Leu Gly Leu Tyr Phe Ser
      20                      25                      30

Arg Asp Ala Tyr Trp Glu Lys Leu Tyr Val Asp Gln Ala Ala Gly Thr
      35                      40                      45

Pro Leu Leu Tyr Val His Ala Leu Arg Asp Ala Pro Glu Glu Val Pro
      50                      55                      60

Ser Phe Arg Leu Gly Gln His Leu Tyr Gly Thr Tyr Arg Thr Arg Leu
      65                      70                      75                      80

His Glu Asn Asn Trp Ile Cys Ile Gln Glu Asp Thr Gly Leu Leu Tyr
      85                      90                      95

Leu Asn Arg Ser Leu Asp His Ser Ser Trp Glu Lys Leu Ser Val Arg
      100                      105                      110

Asn Arg Gly Phe Pro Leu Leu Thr Val Tyr Leu Lys Val Phe Leu Ser
      115                      120                      125

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Pro	Thr	Ser	Leu	Arg	Glu	Gly	Glu	Cys	Gln	Trp	Pro	Gly	Cys	Ala	Arg	130	135	140
Val	Tyr	Phe	Ser	Phe	Phe	Asn	Thr	Ser	Phe	Pro	Ala	Cys	Ser	Ser	Leu	145	150	155
Lys	Pro	Arg	Glu	Leu	Cys	Phe	Pro	Glu	Thr	Arg	Pro	Ser	Phe	Arg	Ile	165	170	175
Arg	Glu	Asn	Arg	Pro	Pro	Gly	Thr	Phe	His	Gln	Phe	Arg	Leu	Leu	Pro	180	185	190
Val	Gln	Phe	Leu	Cys	Pro	Asn	Ile	Ser	Val	Ala	Tyr	Arg	Leu	Leu	Glu	195	200	205
Gly	Glu	Gly	Leu	Pro	Phe	Arg	Cys	Ala	Pro	Asp	Ser	Leu	Glu	Val	Ser	210	215	220
Thr	Arg	Trp	Ala	Leu	Asp	Arg	Glu	Gln	Arg	Glu	Lys	Tyr	Glu	Leu	Val	225	230	235
Ala	Val	Cys	Thr	Val	His	Ala	Gly	Ala	Arg	Glu	Glu	Val	Val	Met	Val	245	250	255
Pro	Phe	Pro	Val	Thr	Val	Tyr	Asp	Glu	Asp	Asp	Ser	Ala	Pro	Thr	Phe	260	265	270
Pro	Ala	Gly	Val	Asp	Thr	Ala	Ser	Ala	Val	Val	Glu	Phe	Lys	Arg	Lys	275	280	285
Glu	Asp	Thr	Val	Val	Ala	Thr	Leu	Arg	Val	Phe	Asp	Ala	Asp	Val	Val	290	295	300
Pro	Ala	Ser	Gly	Glu	Leu	Val	Arg	Arg	Tyr	Thr	Ser	Thr	Leu	Leu	Pro	305	310	315
Gly	Asp	Thr	Trp	Ala	Gln	Gln	Thr	Phe	Arg	Val	Glu	His	Trp	Pro	Asn	325	330	335
Glu	Thr	Ser	Val	Gln	Ala	Asn	Gly	Ser	Phe	Val	Arg	Ala	Thr	Val	His	340	345	350
Asp	Tyr	Arg	Leu	Val	Leu	Asn	Arg	Asn	Leu	Ser	Ile	Ser	Glu	Asn	Arg	355	360	365
Thr	Met	Gln	Leu	Ala	Val	Leu	Val	Asn	Asp	Ser	Asp	Phe	Gln	Gly	Pro	370	375	380
Gly	Ala	Gly	Val	Leu	Leu	Leu	His	Phe	Asn	Val	Ser	Val	Leu	Pro	Val	385	390	395
Ser	Leu	His	Leu	Pro	Ser	Thr	Tyr	Ser	Leu	Ser	Val	Ser	Arg	Arg	Ala	405	410	415
Arg	Arg	Phe	Ala	Gln	Ile	Gly	Lys	Val	Cys	Val	Glu	Asn	Cys	Gln	Ala	420	425	430
Phe	Ser	Gly	Ile	Asn	Val	Gln	Tyr	Lys	Leu	His	Ser	Ser	Gly	Ala	Asn			

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435		440		445
Cys Ser Thr Leu Gly Val Val Thr Ser Ala Glu Asp Thr Ser Gly Ile				
450		455		460
Leu Phe Val Asn Asp Thr Lys Ala Leu Arg Arg Pro Lys Cys Ala Glu				
465		470		480
Leu His Tyr Met Val Val Ala Thr Asp Gln Gln Thr Ser Arg Gln Ala				
	485		490	495
Gln Ala Gln Leu Leu Val Thr Val Glu Gly Ser Tyr Val Ala Glu Glu				
	500		505	510
Ala Gly Cys Pro Leu Ser Cys Ala Val Ser Lys Arg Arg Leu Glu Cys				
	515		520	525
Glu Glu Cys Gly Gly Leu Gly Ser Pro Thr Gly Arg Cys Glu Trp Arg				
	530		535	540
Gln Gly Asp Gly Lys Gly Ile Thr Arg Asn Phe Ser Thr Cys Ser Pro				
	545		550	555
Ser Thr Lys Thr Cys Pro Asp Gly His Cys Asp Val Val Glu Thr Gln				
	565		570	575
Asp Ile Asn Ile Cys Pro Gln Asp Cys Leu Arg Gly Ser Ile Val Gly				
	580		585	590
Gly His Glu Pro Gly Glu Pro Arg Gly Ile Lys Ala Gly Tyr Gly Thr				
	595		600	605
Cys Asn Cys Phe Pro Glu Glu Glu Lys Cys Phe Cys Glu Pro Glu Asp				
	610		615	620
Ile Gln Asp Pro Leu Cys Asp Glu Leu Cys Arg Thr Val Ile Ala Ala				
	625		630	635
Ala Val Leu Phe Ser Phe Ile Val Ser Val Leu Leu Ser Ala Phe Cys				
	645		650	655
Ile His Cys Tyr His Lys Phe Ala His Lys Pro Pro Ile Ser Ser Ala				
	660		665	670
Glu Met Thr Phe Arg Arg Pro Ala Gln Ala Phe Pro Val Ser Tyr Ser				
	675		680	685
Ser Ser Gly Ala Arg Arg Pro Ser Leu Asp Ser Met Glu Asn Gln Val				
	690		695	700
Ser Val Asp Ala Phe Lys Ile Leu Glu Asp Pro Lys Trp Glu Phe Pro				
	705		710	715
Arg Lys Asn Leu Val Leu Gly Lys Thr Leu Gly Glu Gly Glu Phe Gly				
	725		730	735
Lys Val Val Lys Ala Thr Ala Phe His Leu Lys Gly Arg Ala Gly Tyr				
	740		745	750

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Thr	Thr	Val	Ala	Val	Lys	Met	Leu	Lys	Glu	Asn	Ala	Ser	Pro	Ser	Glu
		755					760					765			
Leu	Arg	Asp	Leu	Leu	Ser	Glu	Phe	Asn	Val	Leu	Lys	Gln	Val	Asn	His
	770					775					780				
Pro	His	Val	Ile	Lys	Leu	Tyr	Gly	Ala	Cys	Ser	Gln	Asp	Gly	Pro	Leu
785					790					795					800
Leu	Leu	Ile	Val	Glu	Tyr	Ala	Lys	Tyr	Gly	Ser	Leu	Arg	Gly	Phe	Leu
				805					810					815	
Arg	Glu	Ser	Arg	Lys	Val	Gly	Pro	Gly	Tyr	Leu	Gly	Ser	Gly	Gly	Ser
			820					825					830		
Arg	Asn	Ser	Ser	Ser	Leu	Asp	His	Pro	Asp	Glu	Arg	Ala	Leu	Thr	Met
		835					840					845			
Gly	Asp	Leu	Ile	Ser	Phe	Ala	Trp	Gln	Ile	Ser	Gln	Gly	Met	Gln	Tyr
	850					855					860				
Leu	Ala	Glu	Met	Lys	Leu	Val	His	Arg	Asp	Leu	Ala	Ala	Arg	Asn	Ile
865					870					875					880
Leu	Val	Ala	Glu	Gly	Arg	Lys	Met	Lys	Ile	Ser	Asp	Phe	Gly	Leu	Ser
				885					890					895	
Arg	Asp	Val	Tyr	Glu	Glu	Asp	Ser	Tyr	Val	Lys	Arg	Ser	Gln	Gly	Arg
			900					905					910		
Ile	Pro	Val	Lys	Trp	Met	Ala	Ile	Glu	Ser	Leu	Phe	Asp	His	Ile	Tyr
		915					920					925			
Thr	Thr	Gln	Ser	Asp	Val	Trp	Ser	Phe	Gly	Val	Leu	Leu	Trp	Glu	Ile
		930				935					940				
Val	Thr	Leu	Gly	Gly	Asn	Pro	Tyr	Pro	Gly	Ile	Pro	Pro	Glu	Arg	Leu
945					950					955					960
Phe	Asn	Leu	Leu	Lys	Thr	Gly	His	Arg	Met	Glu	Arg	Pro	Asp	Asn	Cys
				965					970					975	
Ser	Glu	Glu	Met	Tyr	Arg	Leu	Met	Leu	Gln	Cys	Trp	Lys	Gln	Glu	Pro
			980					985					990		
Asp	Lys	Arg	Pro	Val	Phe	Ala	Asp	Ile	Ser	Lys	Asp	Leu	Glu	Lys	Met
		995				1000					1005				
Met	Val	Lys	Arg	Arg	Asp	Tyr	Leu	Asp	Leu	Ala	Ala	Ser	Thr	Pro	Ser
	1010					1015				1020					
Asp	Ser	Leu	Ile	Tyr	Asp	Asp	Gly	Leu	Ser	Glu	Glu	Glu	Thr	Pro	Leu
1025					1030					1035					1040
Val	Asp	Cys	Asn	Asn	Ala	Pro	Leu	Pro	Arg	Ala	Leu	Pro	Ser	Thr	Trp
			1045						1050					1055	

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Ile Glu Asn Lys Leu Tyr Gly Met Ser Asp Pro Asn Trp Pro Gly Glu
 1060 1065 1070

Ser Pro Val Pro Leu Thr Arg Ala Asp Gly Thr Asn Thr Gly Phe Pro
 1075 1080 1085

Arg Tyr Pro Asn Asp Ser Val Tyr Ala Asn Trp Met Leu Ser Pro Ser
 1090 1095 1100

Ala Ala Lys Leu Met Asp Thr Phe Asp Ser
 1105 1110

<210> 278

<211> 393

<212> PRT

<213> Homo sapiens

<400> 278

Met Glu Glu Pro Gln Ser Asp Pro Ser Val Glu Pro Pro Leu Ser Gln
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Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro Glu Asn Asn Val Leu
 20 25 30

Ser Pro Leu Pro Ser Gln Ala Met Asp Asp Leu Met Leu Ser Pro Asp
 35 40 45

Asp Ile Glu Gln Trp Phe Thr Glu Asp Pro Gly Pro Asp Glu Ala Pro
 50 55 60

Arg Met Pro Glu Ala Ala Pro Pro Val Ala Pro Ala Pro Ala Thr Pro
 65 70 75 80

Thr Pro Ala Ala Pro Ala Pro Ala Pro Ser Trp Pro Leu Ser Ser Ser
 85 90 95

Val Pro Ser Gln Lys Thr Tyr Gln Gly Ser Tyr Gly Phe Arg Leu Gly
 100 105 110

Phe Leu His Ser Gly Thr Ala Lys Ser Val Thr Cys Thr Tyr Ser Pro
 115 120 125

Ala Leu Asn Lys Met Phe Cys Gln Leu Ala Lys Thr Cys Pro Val Gln
 130 135 140

Leu Trp Val Asp Ser Thr Pro Pro Pro Gly Thr Arg Val Arg Ala Met
 145 150 155 160

Ala Ile Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys
 165 170 175

Pro His His Glu Arg Cys Ser Asp Ser Asp Gly Leu Ala Pro Pro Gln
 180 185 190

His Leu Ile Arg Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp
 195 200 205

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Arg Asn Thr Phe Arg His Ser Val Val Val Pro Tyr Glu Pro Pro Glu
 210 215 220
 Val Gly Ser Asp Cys Thr Thr Ile His Tyr Asn Tyr Met Cys Asn Ser
 225 230 235 240
 Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr
 245 250 255
 Leu Glu Asp Ser Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val
 260 265 270
 Arg Val Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn
 275 280 285
 Leu Arg Lys Lys Gly Glu Pro His His Glu Leu Pro Pro Gly Ser Thr
 290 295 300
 Lys Arg Ala Leu Pro Asn Asn Thr Ser Ser Ser Pro Gln Pro Lys Lys
 305 310 315 320
 Lys Pro Leu Asp Gly Glu Tyr Phe Thr Leu Gln Ile Arg Gly Arg Glu
 325 330 335
 Arg Phe Glu Met Phe Arg Glu Leu Asn Glu Ala Leu Glu Leu Lys Asp
 340 345 350
 Ala Gln Ala Gly Lys Glu Pro Gly Gly Ser Arg Ala His Ser Ser His
 355 360 365
 Leu Lys Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu Met
 370 375 380
 Phe Lys Thr Glu Gly Pro Asp Ser Asp
 385 390

<210> 279

<211> 1303

<212> DNA

<213> Homo sapiens

<400> 279

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 catggaggag ccgcagtcag atcctagcgt cgagccccct ctgagtcagg aaacattttc 180
 agacctatgg aaactacttc ctgaaaacaa cgttctgtcc cccttgccgt cccaagcaat 240
 ggatgatttg atgctgtccc cggacgatat tgaacaatgg ttcactgaag acccaggtcc 300
 agatgaagct ccagagaatgc cagaggctgc tccccccgtg gcccctgcac cagcgactcc 360
 tacaccggcg gccctgcac cagccccctc ctggccccctg tcatcttctg tcccttccca 420
 gaaaacctac cagggcagct acggtttccg tctgggcttc ttgcattctg ggacagccaa 480
 gtctgtgact tgcacgtact cccctgacct caacaagatg ttttgccaac tggccaagac 540
 ctgcocctgtg cagctgtggg ttgattccac acccccgcgc ggcaccgcgc tccgcgccat 600
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 gcgctgctca gatagcgatg gtctggcccc tcctcagcat cttatccgag tgggaaggaaa 720
 tttgcgtgtg gagtatattg atgacagaaa cacttttcga catagtgtgg tgggtgccta 780
 tgagccgcct gaggttggct ctgactgtac caccatccac tacaactaca tgtgtaacag 840
 ttccctgcatg ggccggcatga accggaggcc catcctcacc atcatcacac tgggaagactc 900

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gaaaccactg gatggagaat atttcaccct tcagatccgt gggcgtgagc gcttcgagat 1140
gttccgagag ctgaatgagg ccttggaact caaggatgcc caggctggga aggagccagg 1200
ggggagcagg gctcactcca gccacctgaa gtccaaaag ggtcagtcta cctcccgcc 1260
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```

<210> 280

<211> 448

<212> PRT

<213> Homo sapiens

<400> 280

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Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
  1                      5                      10          15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
          20                      25          30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
          35                      40          45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
          50                      55          60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
          65                      70          75          80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
          85                      90          95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
          100                     105          110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
          115                     120          125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
          130                     135          140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
          145                     150          155          160

Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
          165                     170          175

Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
          180                     185          190

Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
          195                     200          205

Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
          210                     215          220

Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro

```

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225	230	235	240
Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val			
	245	250	255
Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser			
	260	265	270
Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu			
	275	280	285
Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg			
	290	295	300
Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile			
305	310	315	320
Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys			
	325	330	335
Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys			
	340	345	350
Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly			
	355	360	365
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu			
	370	375	380
Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln			
385	390	395	400
Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys			
	405	410	415
Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser			
	420	425	430
Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro			
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<210> 281

<211> 2816

<212> DNA

<213> Homo sapiens

<400> 281

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aaagaaagtt attaccgatc caccatgtcc cagagcacac agacaaatga attcctcagt 180
ccagagggtt tccagcatat ctgggatttt ctggaacagc ctatatgttc agttcagccc 240
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agcatggact gtatccgcac gcaggactcg gacctgagtg acccatgtg gccacagtac 360
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agtccctata acacagacca cgcgcagaac agcgtcacgg cgccctcgcc ctacgcacag 480
cccagctcca ccttcgatgc tctctctcca tcaccgcgca tcccctccaa caccgactac 540
ccaggccccgc acagtttoga cgtgtccttc cagcagtcga gcaccgcaa gtoggccacc 600

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cagatcaagg tgatgacccc acctcctcag ggagctgtta tccgcgccat gcctgtctac 720
aaaaaagctg agcacgtcac ggaggtggtg aagcgggtgcc ccaaccatga gctgagccgt 780
gaattcaacg agggacagat tgccccctct agtcatttga ttcgagtaga ggggaacagc 840
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caccagcact gtattttctg tcaccaagac aatgatttct tgttattgag gctgttgctt 2760
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<210> 282

<211> 641

<212> PRT

<213> Homo sapiens

<400> 282

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Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
  1                      5                      10                      15

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Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
      20                      25                      30

```

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Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
      35                      40                      45

```

```

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
      50                      55                      60

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Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser

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65	70										75					80				
Met	Asp	Gln	Gln	Ile	Gln	Asn	Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn					
				85					90				95							
Thr	Asp	His	Ala	Gln	Asn	Ser	Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln					
				100					105				110							
Pro	Ser	Ser	Thr	Phe	Asp	Ala	Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser					
				115					120				125							
Asn	Thr	Asp	Tyr	Pro	Gly	Pro	His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln					
				130					135				140							
Ser	Ser	Thr	Ala	Lys	Ser	Ala	Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys					
145					150				155				160							
Lys	Leu	Tyr	Cys	Gln	Ile	Ala	Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val					
				165				170				175								
Met	Thr	Pro	Pro	Pro	Gln	Gly	Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr					
				180				185				190								
Lys	Lys	Ala	Glu	His	Val	Thr	Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His					
				195				200				205								
Glu	Leu	Ser	Arg	Glu	Phe	Asn	Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His					
				210				215				220								
Leu	Ile	Arg	Val	Glu	Gly	Asn	Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro					
225					230				235				240							
Ile	Thr	Gly	Arg	Gln	Ser	Val	Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val					
				245				250				255								
Gly	Thr	Glu	Phe	Thr	Thr	Val	Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser					
				260				265				270								
Cys	Val	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu					
				275				280				285								
Glu	Thr	Arg	Asp	Gly	Gln	Val	Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg					
				290				295				300								
Ile	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile					
305					310				315				320							
Arg	Lys	Gln	Gln	Val	Ser	Asp	Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys					
				325				330				335								
Arg	Pro	Phe	Arg	Gln	Asn	Thr	His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys					
				340				345				350								
Lys	Arg	Arg	Ser	Pro	Asp	Asp	Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly					
				355				360				365								
Arg	Glu	Thr	Tyr	Glu	Met	Leu	Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu					
				370				375				380								

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Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser
 405 410 415
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser
 420 425 430
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg
 435 440 445
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile
 450 455 460
 Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu
 465 470 475 480
 Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser
 485 490 495
 His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly
 500 505 510
 Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr
 515 520 525
 Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp
 530 535 540
 Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys
 545 550 555 560
 Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His
 565 570 575
 Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser
 580 585 590
 Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg
 595 600 605
 Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe
 610 615 620
 Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly
 625 630 635 640

Glu

<210> 283

<211> 2270

<212> DNA

<213> Homo sapiens

<400> 283

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<210> 284

<211> 471

<212> PRT

<213> Homo sapiens

<400> 284

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Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
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Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
      20                      25          30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
  35                      40          45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
  50                      55          60

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Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
 65 70 75 80
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
 85 90 95
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
 100 105 110
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
 115 120 125
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
 130 135 140
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
 145 150 155 160
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
 165 170 175
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
 180 185 190
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200 205
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215 220
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu

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370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser
 405 410 415
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser
 420 425 430
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg
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 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Arg
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 Ser Gly Lys Ser Glu Asn Pro
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<210> 285

<211> 2031

<212> DNA

<213> Homo sapiens

<400> 285

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ccagagggtt tccagcatat ctgggatttt ctggaacagc ctatatgttc agttcagccc 240
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 tcctcccctt cctcttgtct gatttcttag gggaaggaga agtaagaggc tacctcttac 1980
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<210> 286

<211> 416

<212> PRT

<213> Homo sapiens

<400> 286

Met	Leu	Tyr	Leu	Glu	Asn	Asn	Ala	Gln	Thr	Gln	Phe	Ser	Glu	Pro	Gln	1	5	10	15
Tyr	Thr	Asn	Leu	Gly	Leu	Leu	Asn	Ser	Met	Asp	Gln	Gln	Ile	Gln	Asn	20	25	30	
Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn	Thr	Asp	His	Ala	Gln	Asn	Ser	35	40	45	
Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln	Pro	Ser	Ser	Thr	Phe	Asp	Ala	50	55	60	
Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser	Asn	Thr	Asp	Tyr	Pro	Gly	Pro	65	70	75	80
His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln	Ser	Ser	Thr	Ala	Lys	Ser	Ala	85	90	95	
Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys	Lys	Leu	Tyr	Cys	Gln	Ile	Ala	100	105	110	
Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val	Met	Thr	Pro	Pro	Pro	Gln	Gly	115	120	125	
Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr	130	135	140	
Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	Glu	Leu	Ser	Arg	Glu	Phe	Asn	145	150	155	160
Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn	165	170	175	
Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	Ile	Thr	Gly	Arg	Gln	Ser	Val	180	185	190	
Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val	195	200	205	
Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg	210	215	220	
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val	225	230	235	240
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg	245	250	255	

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Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp
 260 265 270
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr
 275 280 285
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp
 290 295 300
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
 305 310 315 320
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His
 325 330 335
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu
 340 345 350
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser
 355 360 365
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val
 370 375 380
 Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr
 385 390 395 400
 Ile Pro Asp Gly Met Gly Ala Asn Arg Ser Gly Lys Ser Glu Asn Pro
 405 410 415

<210> 287

<400> 287

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<210> 288

<211> 461

<212> PRT

<213> Homo sapiens

<400> 288

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
 1 5 10 15
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
 20 25 30
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
 35 40 45
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
 50 55 60
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80

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His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln	Ser	Ser	Thr	Ala	Lys	Ser	Ala	85	90	95
Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys	Lys	Leu	Tyr	Cys	Gln	Ile	Ala	100	105	110
Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val	Met	Thr	Pro	Pro	Pro	Gln	Gly	115	120	125
Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr	130	135	140
Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	Glu	Leu	Ser	Arg	Glu	Phe	Asn	145	150	155
Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn	165	170	175
Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	Ile	Thr	Gly	Arg	Gln	Ser	Val	180	185	190
Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val	195	200	205
Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg	210	215	220
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val	225	230	235
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg	245	250	255
Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp	260	265	270
Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	Arg	Pro	Phe	Arg	Gln	Asn	Thr	275	280	285
His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp	290	295	300
Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	Arg	Glu	Thr	Tyr	Glu	Met	Leu	305	310	315
Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	Met	Gln	Tyr	Leu	Pro	Gln	His	325	330	335
Thr	Ile	Glu	Thr	Tyr	Arg	Gln	Gln	Gln	Gln	Gln	Gln	His	Gln	His	Leu	340	345	350
Leu	Gln	Lys	Gln	Thr	Ser	Ile	Gln	Ser	Pro	Ser	Ser	Tyr	Gly	Asn	Ser	355	360	365
Ser	Pro	Pro	Leu	Asn	Lys	Met	Asn	Ser	Met	Asn	Lys	Leu	Pro	Ser	Val	370	375	380

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Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr
 385 390 395 400
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met
 405 410 415
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro
 420 425 430
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro
 435 440 445
 Tyr Pro Thr Asp Cys Ser Ile Val Gly Ile Trp Gln Val
 450 455 460

<210> 289

 <400> 289
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<210> 290

<211> 586

<212> PRT

<213> Homo sapiens

<400> 290

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
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 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
 20 25 30
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
 35 40 45
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
 50 55 60
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
 85 90 95
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100 105 110
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
 115 120 125
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
 130 135 140
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
 145 150 155 160

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Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn		
				165					170					175			
Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	Ile	Thr	Gly	Arg	Gln	Ser	Val		
			180					185					190				
Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val		
		195					200					205					
Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg		
	210					215					220						
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val		
225					230					235					240		
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg		
				245					250					255			
Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp		
			260					265					270				
Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	Arg	Pro	Phe	Arg	Gln	Asn	Thr		
		275					280					285					
His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp		
	290					295					300						
Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	Arg	Glu	Thr	Tyr	Glu	Met	Leu		
305					310					315					320		
Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	Met	Gln	Tyr	Leu	Pro	Gln	His		
				325					330					335			
Thr	Ile	Glu	Thr	Tyr	Arg	Gln	Gln	Gln	Gln	Gln	Gln	His	Gln	His	Leu		
			340					345					350				
Leu	Gln	Lys	Gln	Thr	Ser	Ile	Gln	Ser	Pro	Ser	Ser	Tyr	Gly	Asn	Ser		
	355						360					365					
Ser	Pro	Pro	Leu	Asn	Lys	Met	Asn	Ser	Met	Asn	Lys	Leu	Pro	Ser	Val		
	370					375					380						
Ser	Gln	Leu	Ile	Asn	Pro	Gln	Gln	Arg	Asn	Ala	Leu	Thr	Pro	Thr	Thr		
385				390						395					400		
Ile	Pro	Asp	Gly	Met	Gly	Ala	Asn	Ile	Pro	Met	Met	Gly	Thr	His	Met		
				405					410					415			
Pro	Met	Ala	Gly	Asp	Met	Asn	Gly	Leu	Ser	Pro	Thr	Gln	Ala	Leu	Pro		
			420					425					430				
Pro	Pro	Leu	Ser	Met	Pro	Ser	Thr	Ser	His	Cys	Thr	Pro	Pro	Pro	Pro		
			435				440					445					
Tyr	Pro	Thr	Asp	Cys	Ser	Ile	Val	Gly	Phe	Leu	Ala	Arg	Leu	Gly	Cys		
	450					455					460						
Ser	Ser	Cys	Leu	Asp	Tyr	Phe	Thr	Thr	Gln	Gly	Leu	Thr	Thr	Ile	Tyr		

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465 470 475 480
 Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro
 485 490 495
 Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln
 500 505 510
 Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser
 515 520 525
 Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val
 530 535 540
 Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro
 545 550 555 560
 Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn
 565 570 575
 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu
 580 585

<210> 291

<400> 291

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<210> 292

<211> 393

<212> PRT

<213> Homo sapiens

<400> 292

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
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 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
 20 25 30
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
 35 40 45
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
 50 55 60
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
 85 90 95
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100 105 110
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly

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115					120					125					
Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr
130						135					140				
Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	Glu	Leu	Ser	Arg	Glu	Phe	Asn
145					150					155					160
Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn
				165					170					175	
Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	Ile	Thr	Gly	Arg	Gln	Ser	Val
			180					185					190		
Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val
		195					200					205			
Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg
	210					215					220				
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val
225						230					235				240
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg
				245					250					255	
Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp
			260					265					270		
Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	Arg	Pro	Phe	Arg	Gln	Asn	Thr
		275					280					285			
His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp
	290					295					300				
Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	Arg	Glu	Thr	Tyr	Glu	Met	Leu
305					310					315					320
Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	Met	Gln	Tyr	Leu	Pro	Gln	His
				325					330					335	
Thr	Ile	Glu	Thr	Tyr	Arg	Gln	Gln	Gln	Gln	Gln	Gln	His	Gln	His	Leu
			340					345					350		
Leu	Gln	Lys	His	Leu	Leu	Ser	Ala	Cys	Phe	Arg	Asn	Glu	Leu	Val	Glu
		355					360					365			
Pro	Arg	Arg	Glu	Thr	Pro	Lys	Gln	Ser	Asp	Val	Phe	Phe	Arg	His	Ser
	370					375					380				
Lys	Pro	Pro	Asn	Arg	Ser	Val	Tyr	Pro							
385					390										

<210> 293

<400> 293

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245/299

<210> 294

<211> 471

<212> PRT

<213> Homo sapiens

<400> 294

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Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
 1           5           10           15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
          20           25           30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
          35           40           45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
 50           55           60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
 65           70           75           80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
          85           90           95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
          100          105          110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
          115          120          125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
          130          135          140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
          145          150          155          160

Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
          165          170          175

Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
          180          185          190

Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
          195          200          205

Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
          210          215          220

Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
          225          230          235          240

Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
          245          250          255

Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
          260          265          270

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Cys	Val	Gly 275	Gly	Met	Asn	Arg	Arg 280	Pro	Ile	Leu	Ile	Ile 285	Val	Thr	Leu
Glu	Thr 290	Arg	Asp	Gly	Gln	Val 295	Leu	Gly	Arg	Arg	Cys 300	Phe	Glu	Ala	Arg
Ile 305	Cys	Ala	Cys	Pro	Gly 310	Arg	Asp	Arg	Lys	Ala 315	Asp	Glu	Asp	Ser	Ile 320
Arg	Lys	Gln	Gln	Val 325	Ser	Asp	Ser	Thr	Lys 330	Asn	Gly	Asp	Gly	Thr 335	Lys
Arg	Pro	Phe 340	Arg	Gln	Asn	Thr	His	Gly 345	Ile	Gln	Met	Thr	Ser 350	Ile	Lys
Lys	Arg	Arg 355	Ser	Pro	Asp	Asp	Glu 360	Leu	Leu	Tyr	Leu	Pro 365	Val	Arg	Gly
Arg	Glu 370	Thr	Tyr	Glu	Met	Leu 375	Leu	Lys	Ile	Lys	Glu 380	Ser	Leu	Glu	Leu
Met 385	Gln	Tyr	Leu	Pro	Gln 390	His	Thr	Ile	Glu	Thr 395	Tyr	Arg	Gln	Gln	Gln 400
Gln	Gln	Gln	His	Gln 405	His	Leu	Leu	Gln	Lys 410	Gln	Thr	Ser	Ile	Gln 415	Ser
Pro	Ser	Ser 420	Tyr	Gly	Asn	Ser	Ser	Pro 425	Pro	Leu	Asn	Lys	Met 430	Asn	Ser
Met	Asn 435	Lys	Leu	Pro	Ser	Val	Ser 440	Gln	Leu	Ile	Asn	Pro 445	Gln	Gln	Arg
Asn	Ala 450	Leu	Thr	Pro	Thr	Thr 455	Ile	Pro	Asp	Gly	Met 460	Gly	Ala	Asn	Arg
Ser 465	Gly	Lys	Ser	Glu	Asn	Pro 470									

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
20 25 30

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Ile	Asp	Leu	Asn	Phe	Val	Asp	Glu	Pro	Ser	Glu	Asp	Gly	Ala	Thr	Asn
		35					40					45			
Lys	Ile	Glu	Ile	Ser	Met	Asp	Cys	Ile	Arg	Met	Gln	Asp	Ser	Asp	Leu
	50					55					60				
Ser	Asp	Pro	Met	Trp	Pro	Gln	Tyr	Thr	Asn	Leu	Gly	Leu	Leu	Asn	Ser
65					70					75					80
Met	Asp	Gln	Gln	Ile	Gln	Asn	Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn
				85					90					95	
Thr	Asp	His	Ala	Gln	Asn	Ser	Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln
			100					105					110		
Pro	Ser	Ser	Thr	Phe	Asp	Ala	Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser
		115					120					125			
Asn	Thr	Asp	Tyr	Pro	Gly	Pro	His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln
	130					135					140				
Ser	Ser	Thr	Ala	Lys	Ser	Ala	Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys
145					150					155					160
Lys	Leu	Tyr	Cys	Gln	Ile	Ala	Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val
				165					170					175	
Met	Thr	Pro	Pro	Pro	Gln	Gly	Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr
			180					185					190		
Lys	Lys	Ala	Glu	His	Val	Thr	Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His
		195					200					205			
Glu	Leu	Ser	Arg	Glu	Phe	Asn	Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His
	210					215					220				
Leu	Ile	Arg	Val	Glu	Gly	Asn	Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro
225					230					235					240
Ile	Thr	Gly	Arg	Gln	Ser	Val	Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val
				245					250					255	
Gly	Thr	Glu	Phe	Thr	Thr	Val	Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser
			260					265					270		
Cys	Val	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu
		275					280					285			
Glu	Thr	Arg	Asp	Gly	Gln	Val	Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg
		290				295					300				
Ile	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile
305					310					315					320
Arg	Lys	Gln	Gln	Val	Ser	Asp	Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys
				325					330					335	

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Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser
 405 410 415
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser
 420 425 430
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg
 435 440 445
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile
 450 455 460
 Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu
 465 470 475 480
 Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser
 485 490 495
 His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly
 500 505 510
 Ile Trp Gln Val
 515

<210> 297

<400> 297

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<210> 298

<211> 641

<212> PRT

<213> Homo sapiens

<400> 298

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
 1 5 10 15
 Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
 20 25 30
 Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
 35 40 45

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Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
 50 55 60
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
 65 70 75 80
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
 85 90 95
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
 100 105 110
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
 115 120 125
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
 130 135 140
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
 145 150 155 160
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
 165 170 175
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
 180 185 190
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200 205
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215 220
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly

250/299

355	360	365
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu		
370	375	380
Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln		
385	390	395
Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser		
405	410	415
Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser		
420	425	430
Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg		
435	440	445
Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile		
450	455	460
Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu		
465	470	475
Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser		
485	490	495
His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly		
500	505	510
Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr		
515	520	525
Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp		
530	535	540
Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys		
545	550	555
Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His		
565	570	575
Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser		
580	585	590
Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg		
595	600	605
Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe		
610	615	620
Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly		
625	630	635
Glu		

<210> 299

251/299

<400> 299
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<210> 300
<211> 448
<212> PRT
<213> Homo sapiens

<400> 300

Met	Ser	Gln	Ser	Thr	Gln	Thr	Asn	Glu	Phe	Leu	Ser	Pro	Glu	Val	Phe
1				5					10					15	
Gln	His	Ile	Trp	Asp	Phe	Leu	Glu	Gln	Pro	Ile	Cys	Ser	Val	Gln	Pro
			20					25					30		
Ile	Asp	Leu	Asn	Phe	Val	Asp	Glu	Pro	Ser	Glu	Asp	Gly	Ala	Thr	Asn
		35					40					45			
Lys	Ile	Glu	Ile	Ser	Met	Asp	Cys	Ile	Arg	Met	Gln	Asp	Ser	Asp	Leu
	50					55					60				
Ser	Asp	Pro	Met	Trp	Pro	Gln	Tyr	Thr	Asn	Leu	Gly	Leu	Leu	Asn	Ser
	65				70					75					80
Met	Asp	Gln	Gln	Ile	Gln	Asn	Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn
				85					90					95	
Thr	Asp	His	Ala	Gln	Asn	Ser	Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln
			100					105					110		
Pro	Ser	Ser	Thr	Phe	Asp	Ala	Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser
		115					120					125			
Asn	Thr	Asp	Tyr	Pro	Gly	Pro	His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln
	130					135					140				
Ser	Ser	Thr	Ala	Lys	Ser	Ala	Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys
	145				150					155					160
Lys	Leu	Tyr	Cys	Gln	Ile	Ala	Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val
			165						170					175	
Met	Thr	Pro	Pro	Pro	Gln	Gly	Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr
			180					185					190		
Lys	Lys	Ala	Glu	His	Val	Thr	Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His
		195					200					205			
Glu	Leu	Ser	Arg	Glu	Phe	Asn	Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His
	210					215					220				
Leu	Ile	Arg	Val	Glu	Gly	Asn	Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro
	225				230					235					240
Ile	Thr	Gly	Arg	Gln	Ser	Val	Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val
				245					250					255	

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Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys
 405 410 415
 Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser
 420 425 430
 Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro
 435 440 445

<210> 301

<400> 301
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<210> 302

<211> 461

<212> PRT

<213> Homo sapiens

<400> 302

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
 1 5 10 15
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
 20 25 30
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
 35 40 45

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Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
 50 55 60
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
 85 90 95
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100 105 110
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
 115 120 125
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
 130 135 140
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
 145 150 155 160
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
 165 170 175
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val
 180 185 190
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val
 195 200 205
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg
 210 215 220
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val
 225 230 235 240
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg
 245 250 255
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp
 260 265 270
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr
 275 280 285
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp
 290 295 300
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
 305 310 315 320
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His
 325 330 335
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu
 340 345 350
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser

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355	360	365
Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val		
370	375	380
Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr		
385	390	395
Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met		
405	410	415
Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro		
420	425	430
Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro		
435	440	445
Tyr Pro Thr Asp Cys Ser Ile Val Arg Ile Trp Gln Val		
450	455	460

<210> 303

<211> 1386

<212> DNA

<213> Homo sapiens

<400> 303

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aacacagacc acgcgagaa cagcgtcacg gcgcccctcg cctacgcaca gccagctcc 180
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gaggacaga ttgcccctcc tagtcatttg attcgagtag aggggaacag ccatgcccag 540
tatgtagaag atcccatcac aggaagacag agtggtgttg taccttatga gccaccccag 600
gttggtcactg aattcacgac agtcttgtac aatttcatgt gtaacagcag ttgtgttgga 660
gggatgaacc gccgtccaat tttaatcatt gttactctgg aaaccagaga tgggcaagtc 720
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gatgaagata gcatcagaaa gcagcaagtt tcggacagta caaagaacgg tgatggtacg 840
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tccccagatg atgaactgtt atacttacca gtgagggggc gtgagactta tgaaatgctg 960
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tacaggcaac agcaacagca gcagcaccag cacttacttc agaaacagac ctcaatacag 1080
tctccatctt catatggtaa cagctcccca cctctgaaca aaatgaacag catgaacaag 1140
ctgccttctg tgagccagct tatcaaccct cagcagcgca acgcccctac tcctacaacc 1200
attcctgatg gcatgggagc caacattccc atgatgggca cccacatgcc aatggctgga 1260
gacatgaatg gactcagccc caccagggca ctccctcccc cactctccat gccatccacc 1320
tccactgca cacccccacc tccgtatccc acagattgca gcattgtcag gatctggcaa 1380
gtctga                                     1386

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<210> 304

<211> 393

<212> PRT

<213> Homo sapiens

255/299

<400> 304

Met	Leu	Tyr	Leu	Glu	Asn	Asn	Ala	Gln	Thr	Gln	Phe	Ser	Glu	Pro	Gln	1	5	10	15
Tyr	Thr	Asn	Leu	Gly	Leu	Leu	Asn	Ser	Met	Asp	Gln	Gln	Ile	Gln	Asn	20	25	30	
Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn	Thr	Asp	His	Ala	Gln	Asn	Ser	35	40	45	
Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln	Pro	Ser	Ser	Thr	Phe	Asp	Ala	50	55	60	
Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser	Asn	Thr	Asp	Tyr	Pro	Gly	Pro	65	70	75	80
His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln	Ser	Ser	Thr	Ala	Lys	Ser	Ala	85	90	95	
Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys	Lys	Leu	Tyr	Cys	Gln	Ile	Ala	100	105	110	
Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val	Met	Thr	Pro	Pro	Pro	Gln	Gly	115	120	125	
Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr	130	135	140	
Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	Glu	Leu	Ser	Arg	Glu	Phe	Asn	145	150	155	160
Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn	165	170	175	
Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	Ile	Thr	Gly	Arg	Gln	Ser	Val	180	185	190	
Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val	195	200	205	
Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg	210	215	220	
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val	225	230	235	240
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg	245	250	255	
Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp	260	265	270	
Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	Arg	Pro	Phe	Arg	Gln	Asn	Thr	275	280	285	
His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp	290	295	300	

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Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
 305 310 315 320
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His
 325 330 335
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu
 340 345 350
 Leu Gln Lys His Leu Leu Ser Ala Cys Phe Arg Asn Glu Leu Val Glu
 355 360 365
 Pro Arg Arg Glu Thr Pro Lys Gln Ser Asp Val Phe Phe Arg His Ser
 370 375 380
 Lys Pro Pro Asn Arg Ser Val Tyr Pro
 385 390

<210> 305

<211> 1182

<212> DNA

<213> Homo sapiens

<400> 305

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aacacagacc acgcgcagaa cagcgtcacc gcgcctcgc cctacgcaca gccagctcc 180
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tatgtagaag atcccatcac aggaagacag agtgtgctgg taccttatga gccaccccag 600
gttggcactg aattcacgac agtctgttac aatttcattg gtaacagcag ttgtgttgga 660
gggatgaacc gccgtccaat tttaatcatt gttactctgg aaaccagaga tgggcaagtc 720
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tcccagatg atgaactggt atacttacca gtgagggggc gtgagactta tgaaatgctg 960
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tacaggcaac agcaacagca gcagcaccag cacttacttc agaaacatct cctttcagcc 1080
tgcttcagga atgagcttgt ggagccccgg agagaaactc caaaacaatc tgacgtcttc 1140
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<210> 306

<211> 586

<212> PRT

<213> Homo sapiens

<400> 306

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
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 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
 20 25 30

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Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn	Thr	Asp	His	Ala	Gln	Asn	Ser	35	40	45
Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln	Pro	Ser	Ser	Thr	Phe	Asp	Ala	50	55	60
Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser	Asn	Thr	Asp	Tyr	Pro	Gly	Pro	65	70	75
His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln	Ser	Ser	Thr	Ala	Lys	Ser	Ala	85	90	95
Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys	Lys	Leu	Tyr	Cys	Gln	Ile	Ala	100	105	110
Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val	Met	Thr	Pro	Pro	Pro	Gln	Gly	115	120	125
Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr	130	135	140
Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	Glu	Leu	Ser	Arg	Glu	Phe	Asn	145	150	155
Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn	165	170	175
Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	Ile	Thr	Gly	Arg	Gln	Ser	Val	180	185	190
Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val	195	200	205
Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg	210	215	220
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val	225	230	235
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg	245	250	255
Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp	260	265	270
Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	Arg	Pro	Phe	Arg	Gln	Asn	Thr	275	280	285
His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp	290	295	300
Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	Arg	Glu	Thr	Tyr	Glu	Met	Leu	305	310	315
Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	Met	Gln	Tyr	Leu	Pro	Gln	His	325	330	335

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Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu
 340 345 350
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser
 355 360 365
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val
 370 375 380
 Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr
 385 390 395 400
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met
 405 410 415
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro
 420 425 430
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro
 435 440 445
 Tyr Pro Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys
 450 455 460
 Ser Ser Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr
 465 470 475 480
 Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro
 485 490 495
 Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln
 500 505 510
 Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser
 515 520 525
 Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val
 530 535 540
 Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro
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 Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn
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 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu
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<210> 307

<211> 1761

<212> DNA

<213> Homo sapiens

<400> 307

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 aacacagacc acgcgcagaa cagcgtcacg ggcgcctcgc cctacgcaca gccagctcc 180

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cacagtttcg acgtgtcctt ccagcagtcg agcaccggcca agtcggccac ctggacgtat 300
tccactgaac tgaagaaact ctactgccaa attgcaaaga catgccccat ccagatcaag 360
gtgatgaccc cacctcctca gggagctgtt atccgcgcca tgcctgtcta caaaaaagct 420
gagcacgtca cggagggtgg gaagcgggtg cccaaccatg agctgagccg tgaattcaac 480
gagggacaga ttgccccctc tagtcatttg attcgagtag agggggaacag ccatgcccag 540
tatgtagaag atcccatcac aggaagacag agtgtgtctg taccttatga gccaccccag 600
gttggcactg aattcacgac agtcttgtac aatttcatgt gtaacagcag ttgtgttgga 660
gggatgaacc gccgtccaat tttaatcatt gttactctgg aaaccagaga tgggcaagtc 720
ctggggccgac gctgctttga ggcccggatc tgtgcttgcc caggaagaga caggaaggcg 780
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<210> 308

<211> 516

<212> PRT

<213> Homo sapiens

<400> 308

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Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
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Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
      20                      25                      30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
      35                      40                      45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
      50                      55                      60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
      65                      70                      75                      80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
      85                      90                      95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
      100                      105                      110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
      115                      120                      125

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Asn	Thr	Asp	Tyr	Pro	Gly	Pro	His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln	130	135	140
Ser	Ser	Thr	Ala	Lys	Ser	Ala	Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys	145	150	155
Lys	Leu	Tyr	Cys	Gln	Ile	Ala	Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val	165	170	175
Met	Thr	Pro	Pro	Pro	Gln	Gly	Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	180	185	190
Lys	Lys	Ala	Glu	His	Val	Thr	Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	195	200	205
Glu	Leu	Ser	Arg	Glu	Phe	Asn	Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	210	215	220
Leu	Ile	Arg	Val	Glu	Gly	Asn	Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	225	230	235
Ile	Thr	Gly	Arg	Gln	Ser	Val	Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	245	250	255
Gly	Thr	Glu	Phe	Thr	Thr	Val	Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	260	265	270
Cys	Val	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	275	280	285
Glu	Thr	Arg	Asp	Gly	Gln	Val	Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	290	295	300
Ile	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	305	310	315
Arg	Lys	Gln	Gln	Val	Ser	Asp	Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	325	330	335
Arg	Pro	Phe	Arg	Gln	Asn	Thr	His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	340	345	350
Lys	Arg	Arg	Ser	Pro	Asp	Asp	Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	355	360	365
Arg	Glu	Thr	Tyr	Glu	Met	Leu	Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	370	375	380
Met	Gln	Tyr	Leu	Pro	Gln	His	Thr	Ile	Glu	Thr	Tyr	Arg	Gln	Gln	Gln	385	390	395
Gln	Gln	Gln	His	Gln	His	Leu	Leu	Gln	Lys	Gln	Thr	Ser	Ile	Gln	Ser	405	410	415
Pro	Ser	Ser	Tyr	Gly	Asn	Ser	Ser	Pro	Pro	Leu	Asn	Lys	Met	Asn	Ser	420	425	430

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Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg
 435 440 445

Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile
 450 455 460

Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu
 465 470 475 480

Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser
 485 490 495

His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Arg
 500 505 510

Ile Trp Gln Val
 515

<210> 309

<211> 1551

<212> DNA

<213> Homo sapiens

<400> 309

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ccatcagaag atggtgcgac aaacaagatt gagattagca tggactgtat ccgcatgcag 180
gactcggacc tgagtgaccc catgtggcca cagtacacga acctggggct cctgaacagc 240
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cagaacagcg tcacggcgcc ctgcacctac gcacagccca gctccacctt cgatgctctc 360
tctccatcac ccgccatccc ctccaacacc gactaccag gcccgcacag tttcgacgtg 420
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gtgggtgaagc ggtgccccaa ccatgagctg agccgtgaat tcaacgaggg acagattgcc 660
cctcctagtc atttgattcg agtagagggg aacagccatg cccagtatgt agaagatccc 720
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ggagccaaca ttcccatgat gggcaccac atgccaatgg ctggagacat gaatggactc 1440
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<210> 310

<211> 641

<212> PRT

<213> Homo sapiens

262/299

<400> 310

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Gln	His	Ile	Trp	Asp	Phe	Leu	Glu	Gln	Pro	Ile	Cys	Ser	Val	Gln	Pro
			20					25					30		
Ile	Asp	Leu	Asn	Phe	Val	Asp	Glu	Pro	Ser	Glu	Asp	Gly	Ala	Thr	Asn
		35					40					45			
Lys	Ile	Glu	Ile	Ser	Met	Asp	Cys	Ile	Arg	Met	Gln	Asp	Ser	Asp	Leu
	50					55					60				
Ser	Asp	Pro	Met	Trp	Pro	Gln	Tyr	Thr	Asn	Leu	Gly	Leu	Leu	Asn	Ser
65					70					75					80
Met	Asp	Gln	Gln	Ile	Gln	Asn	Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn
				85					90					95	
Thr	Asp	His	Ala	Gln	Asn	Ser	Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln
			100					105					110		
Pro	Ser	Ser	Thr	Phe	Asp	Ala	Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser
		115					120					125			
Asn	Thr	Asp	Tyr	Pro	Gly	Pro	His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln
	130					135					140				
Ser	Ser	Thr	Ala	Lys	Ser	Ala	Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys
145					150					155					160
Lys	Leu	Tyr	Cys	Gln	Ile	Ala	Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val
			165						170					175	
Met	Thr	Pro	Pro	Pro	Gln	Gly	Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr
		180						185					190		
Lys	Lys	Ala	Glu	His	Val	Thr	Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His
		195					200					205			
Glu	Leu	Ser	Arg	Glu	Phe	Asn	Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His
	210					215					220				
Leu	Ile	Arg	Val	Glu	Gly	Asn	Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro
225					230					235					240
Ile	Thr	Gly	Arg	Gln	Ser	Val	Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val
			245						250					255	
Gly	Thr	Glu	Phe	Thr	Thr	Val	Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser
		260						265					270		
Cys	Val	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu
		275					280					285			
Glu	Thr	Arg	Asp	Gly	Gln	Val	Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg
	290					295					300				

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Ile	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	305	310	315	320
Arg	Lys	Gln	Gln	Val	Ser	Asp	Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	325	330	335	
Arg	Pro	Phe	Arg	Gln	Asn	Thr	His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	340	345	350	
Lys	Arg	Arg	Ser	Pro	Asp	Asp	Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	355	360	365	
Arg	Glu	Thr	Tyr	Glu	Met	Leu	Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	370	375	380	
Met	Gln	Tyr	Leu	Pro	Gln	His	Thr	Ile	Glu	Thr	Tyr	Arg	Gln	Gln	Gln	385	390	395	400
Gln	Gln	Gln	His	Gln	His	Leu	Leu	Gln	Lys	Gln	Thr	Ser	Ile	Gln	Ser	405	410	415	
Pro	Ser	Ser	Tyr	Gly	Asn	Ser	Ser	Pro	Pro	Leu	Asn	Lys	Met	Asn	Ser	420	425	430	
Met	Asn	Lys	Leu	Pro	Ser	Val	Ser	Gln	Leu	Ile	Asn	Pro	Gln	Gln	Arg	435	440	445	
Asn	Ala	Leu	Thr	Pro	Thr	Thr	Ile	Pro	Asp	Gly	Met	Gly	Ala	Asn	Ile	450	455	460	
Pro	Met	Met	Gly	Thr	His	Met	Pro	Met	Ala	Gly	Asp	Met	Asn	Gly	Leu	465	470	475	480
Ser	Pro	Thr	Gln	Ala	Leu	Pro	Pro	Pro	Leu	Ser	Met	Pro	Ser	Thr	Ser	485	490	495	
His	Cys	Thr	Pro	Pro	Pro	Tyr	Pro	Thr	Asp	Cys	Ser	Ile	Val	Ser		500	505	510	
Phe	Leu	Ala	Arg	Leu	Gly	Cys	Ser	Ser	Cys	Leu	Asp	Tyr	Phe	Thr	Thr	515	520	525	
Gln	Gly	Leu	Thr	Thr	Ile	Tyr	Gln	Ile	Glu	His	Tyr	Ser	Met	Asp	Asp	530	535	540	
Leu	Ala	Ser	Leu	Lys	Ile	Pro	Glu	Gln	Phe	Arg	His	Ala	Ile	Trp	Lys	545	550	555	560
Gly	Ile	Leu	Asp	His	Arg	Gln	Leu	His	Glu	Phe	Ser	Ser	Pro	Ser	His	565	570	575	
Leu	Leu	Arg	Thr	Pro	Ser	Ser	Ala	Ser	Thr	Val	Ser	Val	Gly	Ser	Ser	580	585	590	
Glu	Thr	Arg	Gly	Glu	Arg	Val	Ile	Asp	Ala	Val	Arg	Phe	Thr	Leu	Arg	595	600	605	
Gln	Thr	Ile	Ser	Phe	Pro	Pro	Arg	Asp	Glu	Trp	Asn	Asp	Phe	Asn	Phe				

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610	615	620
Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg	Ile Lys Glu Glu Gly	
625	630	635 640

Glu

<210> 311

<211> 1926

<212> DNA

<213> Homo sapiens

<400> 311

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gagtga
1926

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<210> 312

<211> 448

<212> PRT

<213> Homo sapiens

<400> 312

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Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
 20 25 30
 Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
 35 40 45
 Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
 50 55 60
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
 65 70 75 80
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
 85 90 95
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
 100 105 110
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
 115 120 125
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
 130 135 140
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
 145 150 155 160
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
 165 170 175
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
 180 185 190
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200 205
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215 220
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys

335

Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro
435 440 445

<213> Homo sapiens

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ccagaggttt	tccagcatat	ctgggatttt	ctggaacagc	ctatatgttc	agttcagccc	240
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cagatcaagg	tgatgacccc	acctcctcac	ggagctgtta	tccgcgccat	gcctgtctac	720
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<210> 314

<211> 499

<212> PRT

<213> Homo sapiens

<400> 314

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Gln Ser Ser Arg Gly Asn Asn Glu Val Val Gly Gly Thr Asp Ser Ser
          35              40              45
Met Asp Val Phe His Leu Glu Gly Met Thr Thr Ser Val Met Ala Gln
          50              55              60
Phe Asn Leu Leu Ser Ser Thr Met Asp Gln Met Ser Ser Arg Ala Ala
          65              70              75              80
Ser Ala Ser Pro Tyr Thr Pro Glu His Ala Ala Ser Val Pro Thr His
          85              90              95
Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Thr Met Ser Pro Ala
          100              105              110
Pro Val Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro His His Phe Glu
          115              120              125
Val Thr Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr
          130              135              140
Ser Pro Leu Leu Lys Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro
          145              150              155              160
Ile Gln Ile Lys Val Ser Thr Pro Pro Pro Pro Gly Thr Ala Ile Arg

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Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr	Asp	Val	Val	Lys		
180						185						190					
Arg	Cys	Pro	Asn	His	Glu	Leu	Gly	Arg	Asp	Phe	Asn	Glu	Gly	Gln	Ser		
195						200						205					
Ala	Pro	Ala	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn	Asn	Leu	Ser	Gln		
210						215						220					
Tyr	Val	Asp	Asp	Pro	Val	Thr	Gly	Arg	Gln	Ser	Val	Val	Val	Pro	Tyr		
225						230						235					
Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Ile	Leu	Tyr	Asn	Phe		
245						250						255					
Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu		
260						265						270					
Ile	Ile	Ile	Thr	Leu	Glu	Met	Arg	Asp	Gly	Gln	Val	Leu	Gly	Arg	Arg		
275						280						285					
Ser	Phe	Glu	Gly	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Lys	Ala		
290						295						300					
Asp	Glu	Asp	His	Tyr	Arg	Glu	Gln	Gln	Ala	Leu	Asn	Glu	Ser	Ser	Ala		
305						310						315					
Lys	Asn	Gly	Ala	Ala	Ser	Lys	Arg	Ala	Phe	Lys	Gln	Ser	Pro	Pro	Ala		
325						330						335					
Val	Pro	Ala	Leu	Gly	Ala	Gly	Val	Lys	Lys	Arg	Arg	His	Gly	Asp	Glu		
340						345						350					
Asp	Thr	Tyr	Tyr	Leu	Gln	Val	Arg	Gly	Arg	Glu	Asn	Phe	Glu	Ile	Leu		
355						360						365					
Met	Lys	Leu	Lys	Glu	Ser	Leu	Glu	Leu	Met	Glu	Leu	Val	Pro	Gln	Pro		
370						375						380					
Leu	Val	Asp	Ser	Tyr	Arg	Gln	Gln	Gln	Gln	Leu	Leu	Gln	Arg	Pro	Ser		
385						390						395					
His	Leu	Gln	Pro	Pro	Ser	Tyr	Gly	Pro	Val	Leu	Ser	Pro	Met	Asn	Lys		
405						410						415					
Val	His	Gly	Gly	Met	Asn	Lys	Leu	Pro	Ser	Val	Asn	Gln	Leu	Val	Gly		
420						425						430					
Gln	Pro	Pro	Pro	His	Ser	Ser	Ala	Ala	Thr	Pro	Asn	Leu	Gly	Pro	Val		
435						440						445					
Gly	Pro	Gly	Met	Leu	Asn	Asn	His	Gly	His	Ala	Val	Pro	Ala	Asn	Gly		
450						455						460					
Glu	Met	Ser	Ser	Ser	His	Ser	Ala	Gln	Ser	Met	Val	Ser	Gly	Ser	His		
465						470						475					
												480					

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95

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Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Ile Leu Tyr Asn Phe
 245 250 255
 Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu
 260 265 270
 Ile Ile Ile Thr Leu Glu Met Arg Asp Gly Gln Val Leu Gly Arg Arg
 275 280 285
 Ser Phe Glu Gly Arg Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala
 290 295 300
 Asp Glu Asp His Tyr Arg Glu Gln Gln Ala Leu Asn Glu Ser Ser Ala
 305 310 315 320
 Lys Asn Gly Ala Ala Ser Lys Arg Ala Phe Lys Gln Ser Pro Pro Ala
 325 330 335
 Val Pro Ala Leu Gly Ala Gly Val Lys Lys Arg Arg His Gly Asp Glu
 340 345 350
 Asp Thr Tyr Tyr Leu Gln Val Arg Gly Arg Glu Asn Phe Glu Ile Leu
 355 360 365
 Met Lys Leu Lys Glu Ser Leu Glu Leu Met Glu Leu Val Pro Gln Pro
 370 375 380
 Leu Val Asp Ser Tyr Arg Gln Gln Gln Gln Leu Leu Gln Arg Pro Ser
 385 390 395 400
 His Leu Gln Pro Pro Ser Tyr Gly Pro Val Leu Ser Pro Met Asn Lys
 405 410 415
 Val His Gly Gly Met Asn Lys Leu Pro Ser Val Asn Gln Leu Val Gly
 420 425 430
 Gln Pro Pro Pro His Ser Ser Ala Ala Thr Pro Asn Leu Gly Pro Val
 435 440 445
 Gly Pro Gly Met Leu Asn Asn His Gly His Ala Val Pro Ala Asn Gly
 450 455 460
 Glu Met Ser Ser Ser His Ser Ala Gln Ser Met Val Ser Gly Ser His
 465 470 475 480
 Cys Thr Pro Pro Pro Pro Tyr His Ala Asp Pro Ser Leu Val Ser Phe
 485 490 495
 Leu Thr Gly Leu Gly Cys Pro Asn Cys Ile Glu Tyr Phe Thr Ser Gln
 500 505 510
 Gly Leu Gln Ser Ile Tyr His Leu Gln Asn Leu Thr Ile Glu Asp Leu
 515 520 525
 Gly Ala Leu Lys Ile Pro Glu Gln Tyr Arg Met Thr Ile Trp Arg Gly
 530 535 540
 Leu Gln Asp Leu Lys Gln Gly His Asp Tyr Ser Thr Ala Gln Gln Leu

545	550							555							560	
Leu	Arg	Ser	Ser	Asn	Ala	Ala	Thr	Ile	Ser	Ile	Gly	Gly	Ser	Gly	Glu	
				565					570					575		
Leu	Gln	Arg	Gln	Arg	Val	Met	Glu	Ala	Val	His	Phe	Arg	Val	Arg	His	
				580					585					590		
Thr	Ile	Thr	Ile	Pro	Asn	Arg	Gly	Gly	Pro	Gly	Gly	Gly	Pro	Asp	Glu	
				595					600					605		
Trp	Ala	Asp	Phe	Gly	Phe	Asp	Leu	Pro	Asp	Cys	Lys	Ala	Arg	Lys	Gln	
				610					615					620		
Pro	Ile	Lys	Glu	Glu	Phe	Thr	Glu	Ala	Glu	Ile	His					
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<400> 316															
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Phe	Asn	Leu	Leu	Ser	Ser	Thr	Met	Asp	Gln	Met	Ser	Ser	Arg	Ala	Ala
			20					25					30		
Ser	Ala	Ser	Pro	Tyr	Thr	Pro	Glu	His	Ala	Ala	Ser	Val	Pro	Thr	His
		35					40					45			
Ser	Pro	Tyr	Ala	Gln	Pro	Ser	Ser	Thr	Phe	Asp	Thr	Met	Ser	Pro	Ala
	50					55					60				
Pro	Val	Ile	Pro	Ser	Asn	Thr	Asp	Tyr	Pro	Gly	Pro	His	His	Phe	Glu
65					70					75					80
Val	Thr	Phe	Gln	Gln	Ser	Ser	Thr	Ala	Lys	Ser	Ala	Thr	Trp	Thr	Tyr
				85					90					95	
Ser	Pro	Leu	Leu	Lys	Lys	Leu	Tyr	Cys	Gln	Ile	Ala	Lys	Thr	Cys	Pro
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Ile	Gln	Ile	Lys	Val	Ser	Thr	Pro	Pro	Pro	Pro	Gly	Thr	Ala	Ile	Arg
		115					120					125			
Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr	Asp	Val	Val	Lys
	130					135					140				
Arg	Cys	Pro	Asn	His	Glu	Leu	Gly	Arg	Asp	Phe	Asn	Glu	Gly	Gln	Ser
145				150						155					160
Ala	Pro	Ala	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn	Asn	Leu	Ser	Gln
				165					170					175	
Tyr	Val	Asp	Asp	Pro	Val	Thr	Gly	Arg	Gln	Ser	Val	Val	Val	Pro	Tyr

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180					185					190					
Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Ile	Leu	Tyr	Asn	Phe
		195					200					205			
Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu
	210					215					220				
Ile	Ile	Ile	Thr	Leu	Glu	Met	Arg	Asp	Gly	Gln	Val	Leu	Gly	Arg	Arg
225						230					235				240
Ser	Phe	Glu	Gly	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Lys	Ala
				245					250					255	
Asp	Glu	Asp	His	Tyr	Arg	Glu	Gln	Gln	Ala	Leu	Asn	Glu	Ser	Ser	Ala
			260					265					270		
Lys	Asn	Gly	Ala	Ala	Ser	Lys	Arg	Ala	Phe	Lys	Gln	Ser	Pro	Pro	Ala
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Val	Pro	Ala	Leu	Gly	Ala	Gly	Val	Lys	Lys	Arg	Arg	His	Gly	Asp	Glu
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Asp	Thr	Tyr	Tyr	Leu	Gln	Val	Arg	Gly	Arg	Glu	Asn	Phe	Glu	Ile	Leu
305						310					315				320
Met	Lys	Leu	Lys	Glu	Ser	Leu	Glu	Leu	Met	Glu	Leu	Val	Pro	Gln	Pro
				325					330					335	
Leu	Val	Asp	Ser	Tyr	Arg	Gln	Gln	Gln	Gln	Leu	Leu	Gln	Arg	Pro	Ser
			340				345						350		
His	Leu	Gln	Pro	Pro	Ser	Tyr	Gly	Pro	Val	Leu	Ser	Pro	Met	Asn	Lys
		355					360					365			
Val	His	Gly	Gly	Met	Asn	Lys	Leu	Pro	Ser	Val	Asn	Gln	Leu	Val	Gly
	370					375					380				
Gln	Pro	Pro	Pro	His	Ser	Ser	Ala	Ala	Thr	Pro	Asn	Leu	Gly	Pro	Val
385						390					395				400
Gly	Pro	Gly	Met	Leu	Asn	Asn	His	Gly	His	Ala	Val	Pro	Ala	Asn	Gly
				405					410					415	
Glu	Met	Ser	Ser	Ser	His	Ser	Ala	Gln	Ser	Met	Val	Ser	Gly	Ser	His
			420					425					430		
Cys	Thr	Pro	Pro	Pro	Pro	Tyr	His	Ala	Asp	Pro	Ser	Leu	Val	Ser	Phe
		435					440					445			
Leu	Thr	Gly	Leu	Gly	Cys	Pro	Asn	Cys	Ile	Glu	Tyr	Phe	Thr	Ser	Gln
	450					455					460				
Gly	Leu	Gln	Ser	Ile	Tyr	His	Leu	Gln	Asn	Leu	Thr	Ile	Glu	Asp	Leu
465						470					475				480
Gly	Ala	Leu	Lys	Ile	Pro	Glu	Gln	Tyr	Arg	Met	Thr	Ile	Trp	Arg	Gly
				485					490					495	

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Leu Gln Asp Leu Lys Gln Gly His Asp Tyr Ser Thr Ala Gln Gln Leu
 500 505 510
 Leu Arg Ser Ser Asn Ala Ala Thr Ile Ser Ile Gly Gly Ser Gly Glu
 515 520 525
 Leu Gln Arg Gln Arg Val Met Glu Ala Val His Phe Arg Val Arg His
 530 535 540
 Thr Ile Thr Ile Pro Asn Arg Gly Gly Pro Gly Gly Gly Pro Asp Glu
 545 550 555 560
 Trp Ala Asp Phe Gly Phe Asp Leu Pro Asp Cys Lys Ala Arg Lys Gln
 565 570 575
 Pro Ile Lys Glu Glu Phe Thr Glu Ala Glu Ile His
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<210> 317

<211> 2234

<212> DNA

<213> Homo sapiens

<400> 317

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gcctcaggag gcaggacctt cgggctgtgc ccggggaaag gcaagggtccg gcccattccc 2160
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tcacctgcag aacc                                     2234

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<210> 318

<211> 732

<212> PRT

<213> Homo sapiens

<400> 318

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                20                      25                      30

Ile Ile Asn Thr Phe Tyr Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu
    35                      40                      45

Ile Ser Asn Ser Ser Asp Ala Leu Asp Lys Ile Arg Tyr Glu Thr Leu
    50                      55                      60

Thr Asp Pro Ser Lys Leu Asp Ser Gly Lys Glu Leu His Ile Asn Leu
    65                      70                      75                      80

Ile Pro Asn Lys Gln Asp Arg Thr Leu Thr Ile Val Asp Thr Gly Ile
                85                      90                      95

Gly Met Thr Lys Ala Asp Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys
    100                      105                      110

Ser Gly Thr Lys Ala Phe Met Glu Ala Leu Gln Ala Gly Ala Asp Ile
    115                      120                      125

Ser Met Ile Gly Gln Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val
    130                      135                      140

Ala Glu Lys Val Thr Val Ile Thr Lys His Asn Asp Asp Glu Gln Tyr
    145                      150                      155                      160

Ala Trp Glu Ser Ser Ala Gly Gly Ser Phe Thr Val Arg Thr Asp Thr
                165                      170                      175

Gly Glu Pro Met Gly Arg Gly Thr Lys Val Ile Leu His Leu Lys Glu
    180                      185                      190

Asp Gln Thr Glu Tyr Leu Glu Glu Arg Arg Ile Lys Glu Ile Val Lys
    195                      200                      205

Lys His Ser Gln Phe Ile Gly Tyr Pro Ile Thr Leu Phe Val Glu Lys
    210                      215                      220

Glu Arg Asp Lys Glu Val Ser Asp Asp Glu Ala Glu Glu Lys Glu Asp
    225                      230                      235                      240

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Lys Glu Glu Glu Lys Glu Lys Glu Glu Lys Glu Ser Glu Asp Lys Pro
 245 250 255
 Glu Ile Glu Asp Val Gly Ser Asp Glu Glu Glu Glu Lys Lys Asp Gly
 260 265 270
 Asp Lys Lys Lys Lys Lys Lys Ile Lys Glu Lys Tyr Ile Asp Gln Glu
 275 280 285
 Glu Leu Asn Lys Thr Lys Pro Ile Trp Thr Arg Asn Pro Asp Asp Ile
 290 295 300
 Thr Asn Glu Glu Tyr Gly Glu Phe Tyr Lys Ser Leu Thr Asn Asp Trp
 305 310 315 320
 Glu Asp His Leu Ala Val Lys His Phe Ser Val Glu Gly Gln Leu Glu
 325 330 335
 Phe Arg Ala Leu Leu Phe Val Pro Arg Arg Ala Pro Phe Asp Leu Phe
 340 345 350
 Glu Asn Arg Lys Lys Lys Asn Asn Ile Lys Leu Tyr Val Arg Arg Val
 355 360 365
 Phe Ile Met Asp Asn Cys Glu Glu Leu Ile Pro Glu Tyr Leu Asn Phe
 370 375 380
 Ile Arg Gly Val Val Asp Ser Glu Asp Leu Pro Leu Asn Ile Ser Arg
 385 390 395 400
 Glu Met Leu Gln Gln Ser Lys Ile Leu Lys Val Ile Arg Lys Asn Leu
 405 410 415
 Val Lys Lys Cys Leu Glu Leu Phe Thr Glu Leu Ala Glu Asp Lys Glu
 420 425 430
 Asn Tyr Lys Lys Phe Tyr Glu Gln Phe Ser Lys Asn Ile Lys Leu Gly
 435 440 445
 Ile His Glu Asp Ser Gln Asn Arg Lys Lys Leu Ser Glu Leu Leu Arg
 450 455 460
 Tyr Tyr Thr Ser Ala Ser Gly Asp Glu Met Val Ser Leu Lys Asp Tyr
 465 470 475 480
 Cys Thr Arg Met Lys Glu Asn Gln Lys His Ile Tyr Tyr Ile Thr Gly
 485 490 495
 Glu Thr Lys Asp Gln Val Ala Asn Ser Ala Phe Val Glu Arg Leu Arg
 500 505 510
 Lys His Gly Leu Glu Val Ile Tyr Met Ile Glu Pro Ile Asp Glu Tyr
 515 520 525
 Cys Val Gln Gln Leu Lys Glu Phe Glu Gly Lys Thr Leu Val Ser Val
 530 535 540

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Thr Lys Glu Gly Leu Glu Leu Pro Glu Asp Glu Glu Glu Lys Lys Lys
 545 550 555 560
 Gln Glu Glu Lys Lys Thr Lys Phe Glu Asn Leu Cys Lys Ile Met Lys
 565 570 575
 Asp Ile Leu Glu Lys Lys Val Glu Lys Val Val Val Ser Asn Arg Leu
 580 585 590
 Val Thr Ser Pro Cys Cys Ile Val Thr Ser Thr Tyr Gly Trp Thr Ala
 595 600 605
 Asn Met Glu Arg Ile Met Lys Ala Gln Ala Leu Arg Asp Asn Ser Thr
 610 615 620
 Met Gly Tyr Met Ala Ala Lys Lys His Leu Glu Ile Asn Pro Asp His
 625 630 635 640
 Ser Ile Ile Glu Thr Leu Arg Gln Lys Ala Glu Ala Asp Lys Asn Asp
 645 650 655
 Lys Ser Val Lys Asp Leu Val Ile Leu Leu Tyr Glu Thr Ala Leu Leu
 660 665 670
 Ser Ser Gly Phe Ser Leu Glu Asp Pro Gln Thr His Ala Asn Arg Ile
 675 680 685
 Tyr Arg Met Ile Lys Leu Gly Leu Gly Ile Asp Glu Asp Asp Pro Thr
 690 695 700
 Ala Asp Asp Thr Ser Ala Ala Val Thr Glu Glu Met Pro Pro Leu Glu
 705 710 715 720
 Gly Asp Asp Asp Thr Ser Arg Met Glu Glu Val Asp
 725 730

<210> 319

<211> 249

<212> PRT

<213> Homo sapiens

<400> 319

Met Lys Glu Thr Gln Lys Ser Thr Tyr Tyr Ile Thr Gly Glu Ser Lys
 1 5 10 15
 Glu Gln Val Ala Asn Ser Ala Phe Val Glu Arg Val Arg Lys Gln Gly
 20 25 30
 Phe Glu Val Val Tyr Met Thr Glu Pro Ile Asp Glu Tyr Cys Val Gln
 35 40 45
 Gln Leu Lys Glu Phe Asp Gly Lys Ser Leu Val Ser Val Thr Lys Glu
 50 55 60
 Gly Leu Glu Leu Pro Glu Asp Glu Glu Glu Lys Lys Lys Met Glu Glu
 65 70 75 80

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Ser Lys Glu Lys Phe Glu Asn Leu Cys Lys Leu Met Lys Glu Ile Leu
85 90 95

Asp Lys Lys Val Glu Lys Val Thr Ile Ser Asn Arg Leu Val Ser Ser
100 105 110

Pro Cys Cys Ile Val Thr Ser Thr Tyr Gly Trp Thr Ala Asn Met Glu
115 120 125

Gln Ile Met Lys Ala Gln Ala Leu Arg Asp Asn Ser Thr Met Gly Tyr
130 135 140

Met Met Ala Lys Lys His Leu Glu Ile Asn Pro Asp His Pro Ile Met
145 150 155 160

Glu Thr Leu Arg Gln Lys Ala Glu Ala Asp Lys Asn Asp Lys Ala Val
165 170 175

Lys Asp Leu Val Val Leu Leu Phe Glu Thr Ala Leu Leu Ser Ser Gly
180 185 190

Phe Ser Leu Glu Asp Pro Gln Thr His Ser Asn His Ile Tyr His Met
195 200 205

Ile Lys Leu Gly Leu Gly Thr Asp Glu Asp Glu Val Ala Ala Glu Glu
210 215 220

Pro Ser Asp Ala Val Pro Asp Glu Ile Pro Pro Leu Glu Gly Asp Glu
225 230 235 240

Asp Ala Ser Arg Met Glu Glu Val Asp
245

<210> 320

<211> 1313

<212> DNA

<213> Homo sapiens

<400> 320

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gctggcagaa gacaaggaga ttataagaaa ttctatgagg cattttctaa aaatctcaag 180
cttggaatcc acgaagactc cactaaccgc caccgcctgt ctgagctgct gcgctgtcac 240
acctcccagt ctggagatga gatgacatct ctgtcgtagt atgtttctca catgaaggag 300
acacagaagt ccacctatta catcactggt gagagcaaag agcagggtggc caactctgct 360
tttgtggagc gagtgcggaa acagggcttc gaggtggtat atatgactga gccattgac 420
gagtactgtg tgcagcagct caaggagttt gatgggaaaa gcctggtctc agttaccaag 480
gaggggtctgg agctacctga ggatgaggag gagaagaaga agatggaaga aagcaaggaa 540
aagtttgaga acctctgcaa gctcatgaaa gaaatcttag ataagaaggt tgagaagggtg 600
acaatctcca atagacttgt gtcttcaccc tgctgcattg tgaccagcac ctacggctgg 660
acagccaata tggagcagat catgaaagcc caggcacttc gggacaactc caccatgggc 720
tatatgatgg ccaaaaagca cctggagatc aaccccgacc accccatcat ggagacgctg 780
cggcagaagg ctgaggccga caagaatgat aaggcagtta aggacctggt ggtgctgctg 840
tttgaaaccg ccctgctatc ttcgggcttt tcccttgagg atccccagac ccactccaac 900
cacacttacc acatgatcaa gctaggtcta ggtactgatg aagatgaagt ggcagcagag 960
gaacccagtg atgcagttcc tgatgagatc cccctcttg agggatgatg ggtgctgct 1020
cgcatggaag aagtcgatta ggagttcata gttggaaaac ttgtgccctt gtatagtgtc 1080

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cccatggctc ccactgcagc ctcgagtgcc cctgtccac ctggctgctg gtgtctagt 1140
tttttttccc tctcctgtcc ttgtgttgaa ggcaggaaac caaggggtgc aagccccatt 1200
ccctctctac tcttgacagc aggattggat gttgtgtatt gtggtttatt ttattttctt 1260
cattttgttc tgaaattaaa gaatgtaaaa taaagaatat gccgttttta tac 1313

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<210> 321

<211> 724

<212> PRT

<213> Mus musculus

<400> 321

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Met Pro Glu Glu Val His His Gly Glu Glu Glu Val Glu Thr Phe Ala
  1                      5                      10                      15

Phe Gln Ala Glu Ile Ala Gln Leu Met Ser Leu Ile Ile Asn Thr Phe
          20                      25                      30

Tyr Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ala Ser
          35                      40                      45

Asp Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu Thr Asp Pro Ser Lys
  50                      55                      60

Leu Asp Ser Gly Lys Glu Leu Lys Ile Asp Ile Leu Pro Asn Pro Gln
  65                      70                      75                      80

Glu Arg Thr Leu Thr Leu Val Asp Thr Gly Ile Gly Met Thr Lys Ala
          85                      90                      95

Asp Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Lys Ala
 100                      105                      110

Phe Met Glu Ala Leu Gln Ala Gly Ala Asp Ile Ser Met Ile Gly Gln
 115                      120                      125

Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Glu Lys Val Val
 130                      135                      140

Val Ile Thr Lys His Asn Asp Asp Glu Gln Tyr Ala Trp Glu Ser Ser
 145                      150                      155                      160

Ala Gly Gly Ser Phe Thr Val Arg Ala Asp His Gly Glu Pro Ile Gly
          165                      170                      175

Arg Gly Thr Lys Val Ile Leu His Leu Lys Glu Asp Gln Thr Glu Tyr
          180                      185                      190

Leu Glu Glu Arg Arg Val Lys Glu Val Val Lys Lys His Ser Gln Phe
          195                      200                      205

Ile Gly Tyr Pro Ile Thr Leu Tyr Leu Glu Lys Glu Arg Glu Lys Glu
 210                      215                      220

Ile Ser Asp Asp Glu Ala Glu Glu Glu Lys Gly Glu Lys Glu Glu Glu
 225                      230                      235                      240

Asp Lys Glu Asp Glu Glu Lys Pro Lys Ile Glu Asp Val Gly Ser Asp

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245										250					255				
Glu	Glu	Asp	Asp	Ser	Gly	Lys	Asp	Lys	Lys	Lys	Lys	Thr	Lys	Lys	Ile				
			260					265					270						
Lys	Glu	Lys	Tyr	Ile	Asp	Gln	Glu	Glu	Leu	Asn	Lys	Thr	Lys	Pro	Ile				
		275					280					285							
Trp	Thr	Arg	Asn	Pro	Asp	Asp	Ile	Thr	Gln	Glu	Glu	Tyr	Gly	Glu	Phe				
	290					295					300								
Tyr	Lys	Ser	Leu	Thr	Asn	Asp	Trp	Glu	Asp	His	Leu	Ala	Val	Lys	His				
305					310					315					320				
Phe	Ser	Val	Glu	Gly	Gln	Leu	Glu	Phe	Arg	Ala	Phe	Leu	Phe	Ile	Pro				
				325					330					335					
Arg	Arg	Ala	Pro	Phe	Asp	Leu	Phe	Glu	Asn	Lys	Lys	Lys	Lys	Asn	Asn				
			340					345						350					
Ile	Lys	Leu	Tyr	Val	Arg	Arg	Val	Phe	Ile	Met	Asp	Ser	Cys	Asp	Glu				
		355					360					365							
Leu	Ile	Pro	Glu	Tyr	Leu	Asn	Phe	Ile	Arg	Gly	Val	Val	Asp	Ser	Glu				
	370					375					380								
Asp	Leu	Pro	Leu	Asn	Ile	Ser	Arg	Glu	Met	Leu	Gln	Gln	Ser	Lys	Ile				
385					390					395					400				
Leu	Lys	Val	Ile	Arg	Lys	Asn	Ile	Val	Lys	Lys	Cys	Leu	Glu	Leu	Phe				
				405					410					415					
Ser	Glu	Leu	Ala	Glu	Asp	Lys	Glu	Asn	Tyr	Lys	Lys	Phe	Tyr	Glu	Ala				
			420					425					430						
Phe	Ser	Lys	Asn	Leu	Lys	Leu	Gly	Ile	His	Glu	Asp	Ser	Thr	Asn	Arg				
		435					440					445							
Arg	Arg	Leu	Ser	Glu	Leu	Leu	Arg	Tyr	His	Thr	Ser	Gln	Ser	Gly	Asp				
	450					455					460								
Glu	Met	Thr	Ser	Leu	Ser	Glu	Tyr	Val	Ser	Arg	Met	Lys	Glu	Thr	Gln				
465					470					475					480				
Lys	Ser	Ile	Tyr	Tyr	Ile	Thr	Gly	Glu	Ser	Lys	Glu	Gln	Val	Ala	Asn				
				485					490					495					
Pro	Ala	Phe	Val	Glu	Arg	Val	Arg	Lys	Arg	Gly	Phe	Glu	Val	Val	Tyr				
			500					505					510						
Met	Thr	Glu	Pro	Ile	Asp	Glu	Tyr	Cys	Val	Gln	Gln	Leu	Lys	Glu	Phe				
		515					520					525							
Asp	Gly	Lys	Ser	Leu	Val	Ser	Val	Thr	Lys	Glu	Gly	Leu	Glu	Leu	Pro				
	530					535					540								
Glu	Asp	Glu	Glu	Glu	Lys	Lys	Lys	Met	Glu	Glu	Ser	Lys	Ala	Lys	Phe				
545					550					555					560				

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[illegible]

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<210> 322
<211> 724
<212> PRT
<213> Rattus sp.
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<400> 322

Met	Pro	Glu	Glu	Val	His	His	Gly	Glu	Glu	Glu	Val	Glu	Thr	Phe	Ala
1				5					10					15	
Phe	Gln	Ala	Glu	Ile	Ala	Gln	Leu	Met	Ser	Leu	Ile	Ile	Asn	Thr	Phe
			20					25					30		
Tyr	Ser	Asn	Lys	Glu	Ile	Phe	Leu	Arg	Glu	Leu	Ile	Ser	Asn	Ala	Ser
		35					40					45			
Asp	Ala	Leu	Asp	Lys	Ile	Arg	Tyr	Glu	Ser	Leu	Thr	Asp	Pro	Ser	Lys
	50					55					60				
Leu	Asp	Ser	Gly	Lys	Glu	Leu	Lys	Ile	Asp	Ile	Ile	Pro	Asn	Pro	Gln
65					70					75					80
Glu	Ala	Thr	Leu	Thr	Leu	Val	Asp	Thr	Gly	Ile	Gly	Met	Thr	Lys	Ala
				85					90					95	

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Asp	Leu	Ile	Asn	Asn	Leu	Gly	Thr	Ile	Ala	Lys	Ser	Gly	Thr	Lys	Ala	100	105	110
Phe	Met	Glu	Ala	Leu	Gln	Ala	Gly	Ala	Asp	Ile	Ser	Met	Ile	Gly	Gln	115	120	125
Phe	Gly	Val	Gly	Phe	Tyr	Ser	Ala	Tyr	Leu	Val	Ala	Glu	Lys	Val	Val	130	135	140
Val	Ile	Thr	Lys	His	Asn	Asp	Asp	Glu	Gln	Tyr	Ala	Trp	Glu	Ser	Ser	145	150	155
Ala	Gly	Gly	Ser	Phe	Thr	Val	Arg	Ala	Asp	His	Gly	Glu	Pro	Ile	Gly	165	170	175
Arg	Gly	Thr	Lys	Val	Ile	Leu	His	Leu	Lys	Glu	Asp	Gln	Thr	Glu	Tyr	180	185	190
Leu	Glu	Glu	Arg	Arg	Val	Lys	Glu	Val	Val	Lys	Lys	His	Ser	Gln	Phe	195	200	205
Ile	Gly	Tyr	Pro	Ile	Thr	Leu	Tyr	Leu	Glu	Lys	Glu	Arg	Glu	Lys	Glu	210	215	220
Ile	Ser	Asp	Asp	Glu	Ala	Glu	Glu	Glu	Lys	Gly	Glu	Lys	Glu	Glu	Glu	225	230	235
Asp	Lys	Glu	Asp	Glu	Glu	Lys	Pro	Lys	Ile	Glu	Asp	Val	Gly	Ser	Asp	245	250	255
Glu	Glu	Asp	Asp	Ser	Gly	Lys	Asp	Lys	Lys	Lys	Lys	Thr	Lys	Lys	Ile	260	265	270
Lys	Glu	Lys	Tyr	Ile	Asp	Gln	Glu	Glu	Leu	Asn	Lys	Thr	Lys	Pro	Ile	275	280	285
Trp	Thr	Arg	Asn	Pro	Asp	Asp	Ile	Thr	Gln	Glu	Glu	Tyr	Gly	Glu	Phe	290	295	300
Tyr	Lys	Ser	Leu	Thr	Asn	Asp	Trp	Glu	Asp	His	Leu	Ala	Val	Lys	His	305	310	315
Phe	Ser	Val	Glu	Gly	Gln	Leu	Glu	Phe	Arg	Ala	Leu	Leu	Phe	Ile	Pro	325	330	335
Arg	Arg	Ala	Pro	Phe	Asp	Leu	Phe	Glu	Asn	Lys	Lys	Lys	Lys	Asn	Asn	340	345	350
Ile	Lys	Leu	Tyr	Val	Arg	Arg	Val	Phe	Ile	Met	Asp	Ser	Cys	Asp	Asp	355	360	365
Leu	Ile	Pro	Glu	Tyr	Leu	Asn	Phe	Ile	Arg	Gly	Val	Val	Asp	Ser	Glu	370	375	380
Asp	Leu	Pro	Leu	Asn	Ile	Ser	Arg	Glu	Met	Leu	Gln	Gln	Ser	Lys	Ile	385	390	395
Leu	Lys	Val	Ile	Arg	Lys	Asn	Ile	Val	Lys	Lys	Cys	Leu	Glu	Leu	Phe			

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405										410					415				
Ser	Glu	Leu	Ala	Glu	Asp	Lys	Glu	Asn	Tyr	Lys	Lys	Phe	Tyr	Glu	Ala				
			420					425						430					
Phe	Ser	Lys	Asn	Leu	Lys	Leu	Gly	Ile	His	Glu	Asp	Ser	Thr	Asn	Arg				
		435					440					445							
Arg	Arg	Leu	Ser	Glu	Leu	Leu	Arg	Tyr	His	Thr	Ser	Gln	Ser	Gly	Asp				
	450					455					460								
Glu	Met	Thr	Ser	Leu	Ser	Glu	Tyr	Val	Ser	Arg	Met	Lys	Glu	Thr	Gln				
465					470					475					480				
Lys	Ser	Ile	Tyr	Tyr	Ile	Thr	Gly	Glu	Ser	Lys	Glu	Gln	Val	Ala	Asn				
				485					490					495					
Ser	Ala	Phe	Val	Glu	Arg	Val	Arg	Lys	Arg	Gly	Phe	Glu	Val	Val	Tyr				
			500					505						510					
Met	Thr	Glu	Pro	Ile	Asp	Glu	Tyr	Cys	Val	Gln	Gln	Leu	Lys	Glu	Phe				
		515					520					525							
Asp	Gly	Lys	Ser	Leu	Val	Ser	Val	Thr	Lys	Glu	Gly	Leu	Glu	Leu	Pro				
	530					535					540								
Glu	Asp	Glu	Glu	Glu	Lys	Lys	Lys	Met	Glu	Glu	Ser	Lys	Ala	Arg	Phe				
545					550					555					560				
Glu	Asn	Leu	Cys	Lys	Leu	Met	Lys	Glu	Ile	Leu	Asp	Lys	Lys	Val	Glu				
			565						570					575					
Lys	Val	Thr	Ile	Ser	Asn	Arg	Leu	Val	Ser	Ser	Pro	Cys	Cys	Ile	Val				
			580					585					590						
Thr	Ser	Thr	Tyr	Gly	Trp	Thr	Ala	Asn	Met	Glu	Arg	Ile	Met	Lys	Ala				
		595					600					605							
Gln	Ala	Leu	Arg	Asp	Asn	Ser	Thr	Met	Gly	Tyr	Met	Met	Ala	Lys	Lys				
		610				615					620								
His	Leu	Glu	Ile	Asn	Pro	Asp	His	Pro	Ile	Val	Glu	Thr	Leu	Arg	Gln				
625					630					635					640				
Lys	Ala	Glu	Ala	Asp	Lys	Asn	Asp	Lys	Ala	Val	Lys	Asp	Leu	Val	Val				
			645					650					655						
Leu	Leu	Phe	Glu	Thr	Ala	Leu	Ser	Ser	Leu	Ala	Ser	His	Phe	Arg	Arg				
		660					665						670						
Pro	Lys	Thr	His	Ser	Asn	Arg	Ile	Tyr	Arg	Met	Ile	Lys	Leu	Gly	Leu				
		675				680					685								
Gly	Ile	Asp	Glu	Asp	Glu	Val	Thr	Ala	Glu	Glu	Pro	Ser	Ala	Ala	Val				
	690					695					700								
Pro	Asp	Glu	Ile	Pro	Pro	Leu	Glu	Gly	Asp	Glu	Asp	Ala	Ser	Arg	Met				
705					710						715				720				

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Glu Glu Val Asp

<210> 323

<211> 733

<212> PRT

<213> *Cricetulus griseus*

<400> 323

Met	Pro	Glu	Glu	Thr	Gln	Thr	Gln	Asp	Gln	Pro	Met	Glu	Glu	Glu	Glu
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Val	Glu	Thr	Phe	Ala	Phe	Gln	Ala	Glu	Ile	Ala	Gln	Leu	Met	Ser	Leu
			20					25				30			
Ile	Ile	Asn	Thr	Phe	Tyr	Ser	Asn	Lys	Glu	Ile	Phe	Leu	Arg	Glu	Leu
		35					40					45			
Ile	Ser	Asn	Ser	Ser	Asp	Ala	Leu	Asp	Lys	Ile	Arg	Tyr	Glu	Ser	Leu
	50					55					60				
Thr	Asp	Pro	Ser	Lys	Leu	Asp	Ser	Gly	Lys	Glu	Leu	His	Ile	Asn	Ile
65					70					75					80
Ile	Pro	Asn	Lys	Gln	Asp	Arg	Thr	Leu	Thr	Ile	Val	Asp	Thr	Gly	Ile
				85					90					95	
Gly	Met	Thr	Lys	Ala	Asp	Leu	Ile	Asn	Asn	Leu	Gly	Thr	Ile	Ala	Lys
			100					105					110		
Ser	Gly	Thr	Lys	Ala	Phe	Met	Glu	Ala	Leu	Gln	Ala	Gly	Ala	Asp	Ile
		115					120					125			
Ser	Met	Ile	Gly	Gln	Phe	Gly	Val	Gly	Phe	Tyr	Thr	Ala	Tyr	Leu	Val
	130					135					140				
Ala	Glu	Lys	Val	Thr	Val	Ile	Thr	Lys	His	Asn	Asp	Asp	Glu	Gln	Tyr
145					150					155					160
Ala	Trp	Glu	Ser	Ser	Ala	Gly	Gly	Ser	Phe	Thr	Val	Arg	Thr	Asp	Thr
				165					170					175	
Gly	Glu	Pro	Met	Gly	Arg	Gly	Thr	Lys	Val	Ile	Leu	His	Leu	Lys	Glu
			180					185					190		
Asp	Gln	Thr	Glu	Tyr	Met	Glu	Glu	Arg	Arg	Ile	Lys	Glu	Ile	Val	Lys
		195					200					205			
Lys	His	Ser	Gln	Phe	Ile	Gly	Tyr	Pro	Ile	Thr	Leu	Phe	Val	Glu	Lys
	210					215					220				
Glu	Arg	Asp	Lys	Glu	Val	Ser	Asp	Asp	Glu	Ala	Glu	Glu	Lys	Glu	Asp
225					230					235					240
Lys	Glu	Glu	Glu	Lys	Glu	Lys	Glu	Glu	Lys	Gly	Ile	Asp	Asp	Lys	Pro
				245					250					255	

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Glu Ile Glu Asp Val Gly Ser Asp Glu Glu Glu Glu Glu Lys Lys Asp
 260 265 270
 Gly Asp Lys Lys Lys Lys Lys Lys Ile Lys Glu Lys Tyr Ile Asp Gln
 275 280 285
 Glu Glu Leu Asn Lys Thr Lys Pro Ile Trp Thr Arg Asn Pro Asp Asp
 290 295 300
 Ile Thr Asn Glu Glu Tyr Gly Glu Phe Tyr Lys Ser Leu Thr Asn Asp
 305 310 315 320
 Trp Glu Glu His Leu Ala Val Lys His Phe Ser Val Glu Gly Gln Leu
 325 330 335
 Glu Phe Arg Ala Leu Leu Phe Val Pro Arg Arg Ala Pro Phe Asp Leu
 340 345 350
 Phe Glu Asn Arg Lys Lys Lys Asn Asn Ile Lys Leu Tyr Val Arg Arg
 355 360 365
 Val Phe Ile Met Asp Asn Cys Glu Glu Leu Phe Pro Glu Tyr Leu Asn
 370 375 380
 Phe Ile Arg Gly Val Val Asp Ser Glu Asp Leu Pro Leu Asn Ile Ser
 385 390 395 400
 Arg Glu Ile Leu Gln Gln Ser Lys Ile Leu Lys Val Ile Arg Lys Asn
 405 410 415
 Leu Val Arg Lys Cys Leu Glu Leu Phe His Glu Leu Ala Glu Asp Lys
 420 425 430
 Glu Asn Tyr Lys Lys Phe Tyr Glu Gln Phe Ser Lys Asn Ile Lys Leu
 435 440 445
 Gly Ile His Glu Asp Ser Gln Asn Arg Lys Lys Leu Ser Glu Leu Leu
 450 455 460
 Arg Tyr Tyr Thr Ser Ala Ser Gly Asp Glu Met Val Ser Leu Lys Asp
 465 470 475 480
 Tyr Cys Thr Arg Met Lys Glu Asn Gln Lys His Ile Tyr Phe Ile Thr
 485 490 495
 Gly Glu Thr Lys Asp Gln Val Ala Asn Ser Ala Phe Val Glu Arg Leu
 500 505 510
 Arg Lys His Gly Leu Glu Val Ile Tyr Met Ile Glu Pro Ile Asp Glu
 515 520 525
 Tyr Cys Val Gln Gln Leu Lys Glu Phe Glu Gly Lys Thr Leu Val Ser
 530 535 540
 Val Thr Lys Glu Gly Leu Glu Leu Pro Glu Asp Glu Glu Glu Lys Lys
 545 550 555 560
 Lys Gln Glu Glu Lys Lys Thr Lys Phe Glu Asn Leu Cys Lys Ile Met

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565					570					575					
Lys	Asp	Ile	Leu	Glu	Lys	Lys	Val	Glu	Lys	Val	Val	Val	Ser	Asn	Arg
			580					585					590		
Leu	Val	Thr	Ser	Pro	Cys	Cys	Ile	Val	Thr	Ser	Thr	Tyr	Gly	Trp	Thr
		595					600					605			
Ala	Asn	Met	Glu	Arg	Ile	Ile	Lys	Ala	Gln	Ala	Leu	Arg	Asp	Asn	Ser
	610					615					620				
Thr	Met	Gly	Tyr	Met	Ala	Ala	Lys	Lys	His	Leu	Glu	Ile	Asn	Pro	Asp
625						630					635				640
His	Ser	Ile	Ile	Glu	Thr	Leu	Arg	Gln	Lys	Ala	Glu	Ala	Asp	Lys	Asn
				645					650					655	
Asp	Lys	Ser	Val	Lys	Asp	Leu	Val	Ile	Leu	Leu	Tyr	Glu	Thr	Ala	Leu
			660					665					670		
Leu	Ser	Ser	Gly	Phe	Ser	Leu	Glu	Asp	Pro	Gln	Thr	His	Ala	Asn	Arg
			675					680					685		
Ile	Tyr	Arg	Met	Ile	Lys	Leu	Gly	Leu	Gly	Ile	Asp	Glu	Asp	Asp	Pro
	690					695					700				
Thr	Val	Asp	Asp	Thr	Ser	Ala	Ala	Val	Thr	Glu	Glu	Met	Pro	Pro	Leu
705						710					715				720
Glu	Gly	Asp	Asp	Asp	Thr	Ser	Arg	Met	Glu	Glu	Val	Asp			
				725					730						

<210> 324

<211> 725

<212> PRT

<213> Gallus gallus

<400> 324

Met	Pro	Glu	Gln	Val	Gln	His	Gly	Glu	Asp	Glu	Val	Glu	Thr	Phe	Ala
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Phe	Gln	Ala	Glu	Ile	Ala	Gln	Leu	Met	Ser	Leu	Ile	Ile	Asn	Thr	Phe
			20					25					30		
Tyr	Ser	Asn	Lys	Glu	Ile	Phe	Leu	Arg	Glu	Leu	Ile	Ser	Asn	Ala	Ser
		35					40					45			
Asp	Ala	Leu	Asp	Lys	Ile	Arg	Tyr	Glu	Ser	Leu	Thr	Asp	Pro	Ser	Lys
	50					55					60				
Leu	Asp	Thr	Gly	Lys	Asp	Leu	Lys	Ile	Asp	Ile	Val	Pro	Asn	Pro	Arg
65					70					75					80
Asp	Pro	Thr	Leu	Thr	Leu	Leu	Asp	Thr	Gly	Ile	Gly	Met	Thr	Lys	Ala
				85					90					95	
Asp	Leu	Val	Asn	Asn	Leu	Gly	Thr	Ile	Ala	Lys	Ser	Gly	Thr	Lys	Ala

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100					105					110					
Phe	Met	Glu	Ala	Leu	Gln	Ala	Gly	Ala	Asp	Ile	Ser	Met	Ile	Gly	Gln
		115					120					125			
Phe	Gly	Val	Gly	Phe	Tyr	Ser	Ala	Tyr	Leu	Val	Ala	Glu	Lys	Val	Val
	130					135					140				
Val	Ile	Thr	Lys	His	Asn	Asp	Asp	Glu	Gln	Tyr	Ala	Trp	Glu	Ser	Ser
145					150					155					160
Ala	Gly	Gly	Ser	Phe	Thr	Val	Arg	Thr	Asp	His	Gly	Glu	Pro	Ile	Gly
				165					170					175	
Arg	Gly	Thr	Lys	Val	Ile	Leu	Tyr	Leu	Lys	Glu	Asp	Gln	Thr	Glu	Tyr
			180					185					190		
Leu	Glu	Glu	Arg	Arg	Val	Lys	Glu	Val	Val	Lys	Lys	His	Ser	Gln	Phe
		195					200					205			
Ile	Gly	Tyr	Pro	Ile	Thr	Leu	Tyr	Val	Glu	Lys	Glu	Arg	Glu	Lys	Glu
	210					215					220				
Val	Ser	Asp	Asp	Glu	Ala	Glu	Glu	Glu	Lys	Val	Glu	Lys	Glu	Glu	Glu
225					230					235					240
Glu	Ser	Lys	Asp	Glu	Glu	Lys	Pro	Lys	Ile	Glu	Asp	Val	Gly	Ser	Asp
				245					250					255	
Glu	Glu	Glu	Glu	Glu	Gly	Glu	Lys	Ser	Lys	Lys	Lys	Lys	Thr	Lys	Lys
			260					265					270		
Ile	Lys	Glu	Lys	Tyr	Ile	Asp	Gln	Glu	Glu	Leu	Asn	Lys	Thr	Lys	Pro
		275					280					285			
Ile	Trp	Thr	Arg	Asn	Pro	Asp	Asp	Ile	Thr	Gln	Glu	Glu	Tyr	Gly	Glu
	290					295					300				
Phe	Tyr	Lys	Ser	Leu	Thr	Asn	Asp	Trp	Glu	Asp	His	Leu	Ala	Val	Lys
305					310					315					320
His	Phe	Ser	Val	Glu	Gly	Gln	Leu	Glu	Phe	Arg	Ala	Leu	Leu	Phe	Ile
				325					330					335	
Pro	Arg	Arg	Ala	Pro	Phe	Asp	Leu	Phe	Glu	Asn	Lys	Lys	Lys	Lys	Asn
			340					345					350		
Asn	Ile	Lys	Leu	Tyr	Val	Arg	Arg	Val	Phe	Ile	Met	Asp	Ser	Cys	Asp
		355					360					365			
Glu	Leu	Ile	Pro	Glu	Tyr	Leu	Asn	Phe	Ile	Arg	Gly	Val	Val	Asp	Ser
	370					375					380				
Glu	Asp	Leu	Pro	Leu	Asn	Ile	Ser	Arg	Glu	Met	Leu	Gln	Gln	Ser	Lys
385					390					395					400
Ile	Leu	Lys	Val	Ile	Arg	Lys	Asn	Ile	Val	Lys	Lys	Cys	Leu	Glu	Leu
				405					410					415	

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Phe	Thr	Glu	Leu	Ala	Glu	Asp	Lys	Glu	Asn	Tyr	Lys	Lys	Phe	Tyr	Glu	420	425	430	
Ala	Phe	Ser	Lys	Asn	Leu	Lys	Leu	Gly	Ile	His	Glu	Asp	Ser	Thr	Asn	435	440	445	
Arg	Lys	Arg	Leu	Ser	Glu	Leu	Leu	Arg	Tyr	His	Thr	Ser	Gln	Ser	Gly	450	455	460	
Asp	Glu	Met	Thr	Ser	Leu	Ser	Glu	Tyr	Val	Ser	Arg	Met	Lys	Glu	Ser	465	470	475	480
Gln	Lys	Ser	Ile	Tyr	Tyr	Ile	Thr	Gly	Glu	Ser	Lys	Glu	Gln	Val	Ala	485	490	495	
Asn	Ser	Ala	Phe	Val	Glu	Arg	Val	Arg	Lys	Arg	Gly	Phe	Glu	Val	Val	500	505	510	
Tyr	Met	Thr	Glu	Pro	Ile	Asp	Glu	Tyr	Cys	Val	Gln	Gln	Leu	Lys	Glu	515	520	525	
Phe	Asp	Gly	Lys	Thr	Leu	Val	Ser	Val	Thr	Lys	Glu	Gly	Leu	Glu	Leu	530	535	540	
Pro	Glu	Asp	Glu	Glu	Glu	Lys	Lys	Asn	Met	Glu	Glu	Ser	Lys	Ala	Lys	545	550	555	560
Phe	Glu	Thr	Leu	Cys	Lys	Leu	Met	Lys	Glu	Ile	Leu	Asp	Lys	Lys	Val	565	570	575	
Glu	Lys	Val	Thr	Ile	Ser	Asn	Arg	Leu	Val	Ser	Ser	Pro	Cys	Cys	Ile	580	585	590	
Val	Thr	Ser	Thr	Tyr	Gly	Trp	Thr	Ala	Asn	Met	Glu	Arg	Ile	Met	Lys	595	600	605	
Ala	Gln	Ala	Leu	Arg	Asp	Asn	Ser	Thr	Met	Gly	Tyr	Met	Met	Ala	Lys	610	615	620	
Lys	His	Leu	Glu	Ile	Asn	Pro	Asp	His	Pro	Ile	Val	Glu	Thr	Leu	Arg	625	630	635	640
Gln	Lys	Ala	Asp	Ala	Asn	Lys	Asn	Asp	Lys	Ala	Val	Lys	Asp	Leu	Val	645	650	655	
Val	Leu	Leu	Phe	Glu	Thr	Ala	Leu	Leu	Ser	Ser	Gly	Phe	Ser	Leu	Glu	660	665	670	
Asp	Pro	Gln	Thr	His	Ser	Asn	Arg	Ile	Tyr	Arg	Met	Ile	Lys	Leu	Gly	675	680	685	
Leu	Gly	Ile	Asp	Glu	Asp	Glu	Val	Ile	Ala	Glu	Glu	Ser	Ser	Ile	Ala	690	695	700	
Pro	Pro	Asp	Glu	Ile	Pro	Pro	Leu	Glu	Gly	Asp	Glu	Asp	Thr	Ser	Arg	705	710	715	720

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Met Glu Glu Val Asp
725

<210> 325

<211> 233

<212> PRT

<213> *Sarcophaga crassipalpis*

<400> 325

Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Asp Lys Val Thr
1 5 10 15

Val Thr Ser Lys His Asn Asp Asp Glu Gln Tyr Ile Trp Glu Ser Ser
20 25 30

Ala Gly Gly Ser Phe Thr Val Lys Pro Asp Ser Ser Glu Pro Leu Gly
35 40 45

Arg Gly Thr Lys Ile Val Leu Tyr Ile Lys Glu Asp Gln Thr Glu Tyr
50 55 60

Leu Glu Glu Ser Lys Ile Lys Glu Ile Val Asn Lys His Ser Gln Phe
65 70 75 80

Ile Gly Tyr Pro Ile Lys Leu Leu Val Gln Lys Glu Arg Asp Gln Glu
85 90 95

Val Ser Asp Asp Glu Ala Glu Glu Glu Lys Lys Glu Met Asp Thr Asp
100 105 110

Glu Pro Lys Ile Glu Asp Val Gly Glu Asp Glu Asp Ala Asp Lys Lys
115 120 125

Asp Lys Asp Gly Lys Lys Lys Lys Thr Ile Lys Val Ala Tyr Thr Glu
130 135 140

Asp Glu Glu Leu Asn Lys Thr Lys Pro Ile Trp Thr Arg Asn Pro Asp
145 150 155 160

Asp Ile Thr Gln Ala Glu Tyr Gly Asp Phe Tyr Lys Ser Leu Thr Asn
165 170 175

Asp Trp Glu Asp His Leu Ala Val Lys His Phe Pro Leu Lys Gly Gln
180 185 190

Leu Glu Phe Arg Ala Leu Leu Phe Ile Pro Arg Arg Thr Pro Phe Asp
195 200 205

Leu Phe Glu Asn Gln Lys Lys Arg Asn Asn Ile Lys Leu Tyr Val Pro
210 215 220

Arg Val Phe Ile Met Asp Asn Cys Glu
225 230

<210> 326

<211> 724

289/299

<212> PRT

<213> Danio rerio

<400> 326

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Met Pro Glu Glu Met Arg Gln Glu Glu Glu Ala Glu Thr Phe Ala Phe
  1           5           10           15

Gln Ala Glu Ile Ala Gln Leu Met Ser Leu Ile Ile Asn Thr Phe Tyr
      20           25           30

Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Val Ser Asn Ala Ser Asp
      35           40           45

Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu Thr Asp Pro Thr Lys Leu
      50           55           60

Asp Ser Gly Lys Asp Leu Lys Ile Asp Ile Ile Pro Asn Val Gln Glu
      65           70           75           80

Arg Thr Leu Thr Leu Ile Asp Thr Gly Ile Gly Met Thr Lys Ala Asp
      85           90           95

Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Lys Ala Phe
      100          105          110

Met Glu Ala Leu Gln Ala Gly Ala Asp Ile Ser Met Ile Gly Gln Phe
      115          120          125

Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Glu Lys Val Thr Val
      130          135          140

Ile Thr Lys His Asn Asp Asp Glu Gln Tyr Ala Trp Glu Ser Ser Ala
      145          150          155          160

Gly Gly Ser Phe Thr Val Lys Val Asp His Gly Glu Pro Ile Gly Arg
      165          170          175

Gly Thr Lys Val Ile Leu His Leu Lys Glu Asp Gln Thr Glu Tyr Ile
      180          185          190

Glu Glu Lys Arg Val Lys Glu Val Val Lys Lys His Ser Gln Phe Ile
      195          200          205

Gly Tyr Pro Ile Thr Leu Tyr Val Glu Lys Glu Arg Asp Lys Glu Ile
      210          215          220

Ser Asp Asp Glu Ala Glu Glu Glu Lys Ala Glu Lys Glu Glu Lys Glu
      225          230          235          240

Glu Glu Gly Glu Asp Lys Pro Lys Ile Glu Asp Val Gly Ser Asp Asp
      245          250          255

Glu Glu Asp Thr Lys Asp Lys Asp Lys Lys Lys Lys Lys Lys Ile Lys
      260          265          270

Glu Lys Tyr Ile Asp Gln Glu Glu Leu Asn Lys Thr Lys Pro Ile Trp
      275          280          285

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Thr Arg Asn Pro Asp Asp Ile Ser Asn Glu Glu Tyr Gly Glu Phe Tyr
 290 295 300
 Lys Ser Leu Thr Asn Asp Trp Glu Asp His Leu Ala Val Lys His Phe
 305 310 315 320
 Ser Val Glu Gly Gln Leu Glu Phe Arg Ala Leu Leu Phe Ile Pro Arg
 325 330 335
 Arg Ala Pro Phe Asp Leu Phe Glu Asn Lys Lys Lys Lys Asn Asn Ile
 340 345 350
 Lys Leu Tyr Val Arg Arg Val Phe Ile Met Asp Asn Cys Glu Glu Leu
 355 360 365
 Ile Pro Glu Tyr Leu Asn Phe Ile Arg Gly Val Val Asp Ser Glu Asp
 370 375 380
 Leu Pro Leu Asn Ile Ser Arg Glu Met Leu Gln Gln Ser Lys Ile Leu
 385 390 395 400
 Lys Val Ile Arg Lys Asn Ile Val Lys Lys Cys Leu Glu Leu Phe Ala
 405 410 415
 Asp Val Ala Glu Asp Lys Asp Asn Tyr Lys Lys Phe Tyr Asp Ala Phe
 420 425 430
 Ser Lys Asn Leu Lys Leu Gly Ile His Glu Asp Ser Gln Asn Arg Arg
 435 440 445
 Lys Leu Ser Glu Leu Leu Arg Tyr Gln Ser Ser Gln Ser Gly Tyr Glu
 450 455 460
 Met Thr Ser Leu Thr Glu Tyr Val Ser Arg Met Lys Glu Asn Gln Lys
 465 470 475 480
 Ser Ile Tyr Tyr Ile Thr Gly Glu Ser Lys Asp Gln Val Ala His Ser
 485 490 495
 Ala Phe Val Glu Arg Val Cys Lys Arg Gly Phe Glu Val Leu Tyr Met
 500 505 510
 Thr Glu Pro Ile Asp Glu Tyr Cys Val Gln Gln Leu Lys Asp Phe Asp
 515 520 525
 Gly Lys Ser Leu Val Ser Val Thr Lys Glu Gly Leu Glu Leu Pro Glu
 530 535 540
 Asp Glu Asp Glu Lys Lys Lys Met Glu Glu Asp Lys Ala Lys Phe Glu
 545 550 555 560
 Asn Leu Cys Lys Leu Met Lys Glu Ile Leu Asp Lys Lys Val Glu Lys
 565 570 575
 Val Thr Val Ser Asn Arg Leu Val Ser Ser Pro Cys Cys Ile Val Thr
 580 585 590
 Ser Thr Tyr Gly Trp Thr Ala Asn Met Glu Arg Ile Met Lys Ala Gln

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595	600	605
Ala Leu Arg Asp Asn Ser Thr Met Gly Tyr Met Met Ala Lys Lys His		
610	615	620
Leu Glu Ile Asn Pro Asp His Pro Ile Met Glu Thr Leu Arg Gln Lys		
625	630	635 640
Ala Glu Ala Asp Lys Asn Asp Lys Ala Val Lys Asp Leu Val Ile Leu		
	645	650 655
Leu Phe Glu Thr Ala Leu Leu Ser Ser Gly Phe Ser Leu Asp Asp Pro		
	660	665 670
Gln Thr His Ser Asn Arg Ile Tyr Arg Met Ile Lys Leu Gly Leu Gly		
	675	680 685
Ile Asp Glu Asp Glu Asp Val Pro Val Glu Glu Pro Ser Ser Ala Ala		
	690	695 700
Pro Glu Asp Ile Pro Pro Leu Glu Gly Asp Asp Asp Ala Ser Arg Met		
705	710	715 720
Glu Glu Val Asp		

<210> 327

<211> 722

<212> PRT

<213> Salmo salar

<400> 327

Met Pro Glu Glu Met Arg Gln Glu Glu Glu Ala Glu Thr Phe Ala Phe	
1 5 10 15	
Gln Ala Glu Ile Ala Gln Leu Met Ser Leu Ile Ile Asn Thr Phe Tyr	
20 25 30	
Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ala Ser Asp	
35 40 45	
Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu Thr Asp Pro Thr Lys Leu	
50 55 60	
Asp Asn Gly Lys Glu Leu Lys Ile Asp Val Ile Pro Asn Val Glu Glu	
65 70 75 80	
Arg Thr Leu Thr Leu Ile Asp Thr Gly Ile Gly Met Thr Lys Ala Asp	
85 90 95	
Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Lys Ala Phe	
100 105 110	
Met Glu Ala Leu Gln Ala Gly Ala Asp Ile Ser Met Ile Gly Gln Phe	
115 120 125	
Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Glu Arg Val Thr Val	
130 135 140	

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Ile	Thr	Lys	His	Asn	Asp	Asp	Glu	Gln	Tyr	Ile	Trp	Glu	Ser	Ser	Ala	145	150	155	160
Gly	Gly	Ser	Phe	Thr	Val	Lys	Val	Asp	Thr	Gly	Glu	Pro	Met	Leu	Arg	165	170	175	
Gly	Thr	Lys	Val	Ile	Leu	His	Met	Lys	Glu	Asp	Gln	Thr	Glu	Tyr	Val	180	185	190	
Glu	Glu	Lys	Arg	Val	Lys	Glu	Val	Val	Lys	Lys	His	Ser	Gln	Phe	Ile	195	200	205	
Gly	Tyr	Pro	Ile	Thr	Leu	Phe	Val	Glu	Lys	Glu	Arg	Glu	Lys	Glu	Ile	210	215	220	
Ser	Asp	Asp	Glu	Glu	Glu	Lys	Ala	Glu	Glu	Glu	Lys	Glu	Glu	Lys	Glu	225	230	235	240
Ala	Glu	Asp	Lys	Pro	Lys	Ile	Glu	Asp	Val	Gly	Ser	Asp	Asp	Glu	Glu	245	250	255	
Asp	Ser	Lys	Asp	Lys	Asp	Lys	Lys	Lys	Thr	Lys	Lys	Ile	Lys	Glu	Lys	260	265	270	
Tyr	Ile	Asp	Gln	Glu	Glu	Leu	Asn	Lys	Thr	Lys	Pro	Ile	Trp	Thr	Arg	275	280	285	
Asn	Pro	Asp	Asp	Ile	Thr	Met	Glu	Glu	Tyr	Gly	Glu	Phe	Tyr	Lys	Ser	290	295	300	
Leu	Thr	Asn	Asp	Trp	Glu	Glu	His	Leu	Ala	Val	Lys	His	Phe	Ser	Val	305	310	315	320
Glu	Gly	Gln	Leu	Glu	Phe	Arg	Ala	Leu	Leu	Phe	Ile	Pro	Arg	Arg	Ala	325	330	335	
Pro	Phe	Asp	Leu	Phe	Glu	Asn	Lys	Lys	Lys	Lys	Asn	Asn	Ile	Lys	Leu	340	345	350	
Tyr	Val	Arg	Arg	Val	Phe	Ile	Met	Asp	Ser	Cys	Glu	Glu	Leu	Ile	Pro	355	360	365	
Glu	Tyr	Leu	Asn	Phe	Val	Arg	Gly	Val	Val	Asp	Ser	Glu	Asp	Leu	Pro	370	375	380	
Leu	Asn	Ile	Ser	Arg	Glu	Met	Leu	Gln	Gln	Ser	Lys	Ile	Leu	Lys	Val	385	390	395	400
Ile	Arg	Lys	Asn	Ile	Val	Lys	Lys	Cys	Met	Glu	Leu	Phe	Gly	Glu	Leu	405	410	415	
Ala	Glu	Asp	Arg	Glu	Asn	Tyr	Asn	Lys	Phe	Tyr	Asp	Gly	Phe	Ser	Lys	420	425	430	
Asn	Leu	Lys	Leu	Gly	Ile	His	Glu	Asp	Ser	Gln	Asn	Arg	Lys	Lys	Leu	435	440	445	

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Ser Glu Leu Leu Arg Tyr His Ser Ser Gln Ser Gly Asp Glu Leu Thr
 450 455 460
 Ser Leu Thr Glu Tyr Leu Thr Arg Met Lys Asp Asn Gln Lys Ser Ile
 465 470 475 480
 Tyr Tyr Ile Thr Gly Glu Ser Lys Asp Gln Val Ala Asn Ser Ala Phe
 485 490 495
 Val Glu Arg Val Arg Lys Arg Gly Phe Glu Val Leu Tyr Met Thr Glu
 500 505 510
 Pro Ile Asp Glu Tyr Cys Val Gln Gln Leu Lys Glu Phe Asp Gly Lys
 515 520 525
 Thr Leu Val Ser Val Thr Lys Glu Gly Leu Glu Leu Pro Glu Asp Glu
 530 535 540
 Glu Glu Lys Lys Lys Met Asp Glu Asp Lys Thr Lys Phe Glu Asn Leu
 545 550 555 560
 Cys Lys Leu Met Lys Glu Ile Leu Asp Lys Lys Val Glu Lys Val Thr
 565 570 575
 Val Ser Asn Arg Leu Val Ser Ser Pro Cys Cys Ile Val Thr Ser Thr
 580 585 590
 Tyr Gly Trp Thr Ala Asn Met Glu Arg Ile Met Lys Ala Gln Ala Leu
 595 600 605
 Arg Asp Asn Ser Thr Met Gly Tyr Met Met Ala Lys Lys His Leu Glu
 610 615 620
 Ile Asn Pro Asp His Pro Ile Val Glu Thr Leu Arg Gln Lys Ala Asp
 625 630 635 640
 Leu Asp Lys Asn Asp Lys Ala Val Lys Asp Leu Val Ile Leu Leu Phe
 645 650 655
 Glu Thr Ala Leu Leu Ser Ser Gly Phe Ser Leu Asp Asp Pro Gln Thr
 660 665 670
 His Ser Asn Arg Ile Tyr Arg Met Ile Lys Leu Gly Leu Gly Ile Asp
 675 680 685
 Asp Asp Glu Val Ile Pro Glu Glu Pro Thr Ser Ala Pro Ala Pro Asp
 690 695 700
 Glu Ile Pro Pro Leu Glu Gly Asp Asp Asp Ala Ser Arg Met Glu Glu
 705 710 715 720

Val Asp

<210> 328

<211> 733

<212> PRT

<213> Sus scrofa

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<400> 328

Met	Pro	Glu	Glu	Thr	Gln	Thr	Gln	Asp	Gln	Pro	Met	Glu	Glu	Glu	Glu	1	5	10	15
Val	Glu	Thr	Phe	Ala	Phe	Gln	Ala	Glu	Ile	Ala	Gln	Leu	Met	Ser	Leu	20	25	30	
Ile	Ile	Asn	Thr	Phe	Tyr	Ser	Asn	Lys	Glu	Ile	Phe	Leu	Arg	Glu	Leu	35	40	45	
Ile	Ser	Asn	Ser	Ser	Asp	Ala	Leu	Asp	Lys	Ile	Arg	Tyr	Glu	Ser	Leu	50	55	60	
Thr	Asp	Pro	Ser	Lys	Leu	Asp	Ser	Gly	Lys	Glu	Leu	His	Ile	Asn	Leu	65	70	75	80
Ile	Pro	Asn	Lys	Gln	Asp	Arg	Thr	Leu	Thr	Ile	Val	Asp	Thr	Gly	Ile	85	90	95	
Gly	Met	Thr	Lys	Ala	Asp	Leu	Ile	Asn	Asn	Leu	Gly	Thr	Ile	Ala	Lys	100	105	110	
Ser	Gly	Thr	Lys	Ala	Phe	Met	Glu	Ala	Leu	Gln	Ala	Gly	Ala	Asp	Ile	115	120	125	
Ser	Met	Ile	Gly	Gln	Phe	Gly	Val	Gly	Phe	Tyr	Ser	Ala	Tyr	Leu	Val	130	135	140	
Ala	Glu	Lys	Val	Thr	Val	Ile	Thr	Lys	His	Asn	Asp	Asp	Glu	Gln	Tyr	145	150	155	160
Ala	Trp	Glu	Ser	Ser	Ala	Gly	Gly	Ser	Phe	Thr	Val	Arg	Thr	Asp	Thr	165	170	175	
Gly	Glu	Pro	Met	Gly	Arg	Gly	Thr	Lys	Val	Ile	Leu	His	Leu	Lys	Glu	180	185	190	
Asp	Gln	Thr	Glu	Tyr	Leu	Glu	Glu	Arg	Arg	Ile	Lys	Glu	Ile	Val	Lys	195	200	205	
Lys	His	Ser	Gln	Phe	Ile	Gly	Tyr	Pro	Ile	Thr	Leu	Phe	Val	Glu	Lys	210	215	220	
Glu	Arg	Asp	Lys	Glu	Val	Ser	Asp	Asp	Glu	Ala	Glu	Glu	Lys	Glu	Asp	225	230	235	240
Lys	Glu	Glu	Glu	Lys	Glu	Lys	Glu	Glu	Lys	Glu	Ser	Glu	Asp	Lys	Pro	245	250	255	
Glu	Ile	Glu	Asp	Val	Gly	Ser	Asp	Glu	Glu	Glu	Glu	Glu	Lys	Lys	Asp	260	265	270	
Gly	Asp	Lys	Lys	Lys	Lys	Lys	Lys	Ile	Lys	Glu	Lys	Tyr	Ile	Asp	Gln	275	280	285	
Glu	Glu	Leu	Asn	Lys	Thr	Lys	Pro	Ile	Trp	Thr	Arg	Asn	Pro	Asp	Asp	290	295	300	

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Ile	Thr	Asn	Glu	Glu	Tyr	Gly	Glu	Phe	Tyr	Lys	Ser	Leu	Thr	Asn	Asp	
305					310					315					320	
Trp	Glu	Asp	His	Leu	Ala	Val	Lys	His	Phe	Ser	Val	Glu	Gly	Gln	Leu	
				325					330					335		
Glu	Phe	Arg	Ala	Leu	Leu	Phe	Val	Pro	Arg	Arg	Ala	Pro	Phe	Asp	Leu	
			340					345					350			
Phe	Glu	Asn	Arg	Lys	Lys	Lys	Asn	Asn	Ile	Lys	Leu	Tyr	Val	Arg	Arg	
		355					360					365				
Val	Phe	Ile	Met	Asp	Asn	Cys	Glu	Glu	Leu	Ile	Pro	Glu	Tyr	Leu	Asn	
	370					375					380					
Phe	Ile	Arg	Gly	Val	Val	Asp	Ser	Glu	Asp	Leu	Pro	Leu	Asn	Ile	Ser	
385					390					395					400	
Arg	Glu	Met	Leu	Gln	Gln	Ser	Lys	Ile	Leu	Lys	Val	Ile	Arg	Lys	Asn	
				405					410						415	
Leu	Val	Lys	Lys	Cys	Leu	Glu	Leu	Phe	Thr	Glu	Leu	Ala	Glu	Asp	Lys	
			420					425					430			
Glu	Asn	Tyr	Lys	Lys	Phe	Tyr	Glu	Gln	Phe	Ser	Lys	Asn	Ile	Lys	Leu	
		435					440					445				
Gly	Ile	His	Glu	Asp	Ser	Gln	Asn	Arg	Lys	Lys	Leu	Ser	Glu	Leu	Leu	
	450					455					460					
Arg	Tyr	Tyr	Thr	Ser	Ala	Ser	Gly	Asp	Glu	Met	Val	Ser	Leu	Lys	Asp	
465					470					475					480	
Tyr	Cys	Thr	Arg	Met	Lys	Glu	Asn	Gln	Lys	His	Ile	Tyr	Tyr	Ile	Thr	
				485					490					495		
Gly	Glu	Thr	Lys	Asp	Gln	Val	Ala	Asn	Ser	Ala	Phe	Val	Glu	Arg	Leu	
			500					505					510			
Arg	Lys	His	Gly	Leu	Glu	Val	Ile	Tyr	Met	Ile	Glu	Pro	Ile	Asp	Glu	
		515					520					525				
Tyr	Cys	Val	Gln	Gln	Leu	Lys	Glu	Phe	Glu	Gly	Lys	Thr	Leu	Val	Ser	
		530				535					540					
Val	Thr	Lys	Glu	Gly	Leu	Glu	Leu	Pro	Glu	Asp	Glu	Glu	Glu	Lys	Lys	
545					550					555					560	
Lys	Gln	Glu	Glu	Lys	Lys	Thr	Lys	Phe	Glu	Asn	Leu	Cys	Lys	Ile	Met	
				565					570					575		
Lys	Asp	Ile	Leu	Glu	Lys	Lys	Val	Glu	Lys	Val	Val	Val	Ser	Asn	Arg	
			580					585					590			
Leu	Val	Thr	Ser	Pro	Cys	Cys	Ile	Val	Thr	Ser	Thr	Tyr	Gly	Trp	Thr	
		595					600					605				

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Ala Asn Met Glu Arg Ile Met Lys Ala Gln Ala Leu Arg Asp Asn Ser
610 615 620

Thr Met Gly Tyr Met Ala Ala Lys Lys His Leu Glu Ile Asn Pro Asp
625 630 635 640

His Ser Ile Ile Glu Thr Leu Arg Gln Lys Ala Glu Ala Asp Lys Asn
645 650 655

Asp Lys Ser Val Lys Asp Leu Val Ile Leu Leu Tyr Glu Thr Ala Leu
660 665 670

Leu Ser Ser Gly Phe Ser Leu Glu Asp Pro Gln Thr His Ala Asn Arg
675 680 685

Ile Tyr Arg Met Ile Lys Leu Gly Leu Gly Ile Asp Glu Asp Asp Pro
690 695 700

Thr Ala Asp Asp Ser Ser Ala Ala Val Thr Glu Glu Met Pro Pro Leu
705 710 715 720

Glu Gly Asp Asp Asp Thr Ser Arg Met Glu Glu Val Asp
725 730

<210> 329

<211> 709

<212> PRT.

<213> *Saccharomyces cerevisiae*

<400> 329

Met Ala Ser Glu Thr Phe Glu Phe Gln Ala Glu Ile Thr Gln Leu Met
1 5 10 15

Ser Leu Ile Ile Asn Thr Val Tyr Ser Asn Lys Glu Ile Phe Leu Arg
20 25 30

Glu Leu Ile Ser Asn Ala Ser Asp Ala Leu Asp Lys Ile Arg Tyr Lys
35 40 45

Ser Leu Ser Asp Pro Lys Gln Leu Glu Thr Glu Pro Asp Leu Phe Ile
50 55 60

Arg Ile Thr Pro Lys Pro Glu Gln Lys Val Leu Glu Ile Arg Asp Ser
65 70 75 80

Gly Ile Gly Met Thr Lys Ala Glu Leu Ile Asn Asn Leu Gly Thr Ile
85 90 95

Ala Lys Ser Gly Thr Lys Ala Phe Met Glu Ala Leu Ser Ala Gly Ala
100 105 110

Asp Val Ser Met Ile Gly Gln Phe Gly Val Gly Phe Tyr Ser Leu Phe
115 120 125

Leu Val Ala Asp Arg Val Gln Val Ile Ser Lys Ser Asn Asp Asp Glu
130 135 140

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Gln Tyr Ile Trp Glu Ser Asn Ala Gly Gly Ser Phe Thr Val Thr Leu
 145 150 155 160
 Asp Glu Val Asn Glu Arg Ile Gly Arg Gly Thr Ile Leu Arg Leu Phe
 165 170 175
 Leu Lys Asp Asp Gln Leu Glu Tyr Leu Glu Glu Lys Arg Ile Lys Glu
 180 185 190
 Val Ile Lys Arg His Ser Glu Phe Val Ala Tyr Pro Ile Gln Leu Val
 195 200 205
 Val Thr Lys Glu Val Glu Lys Glu Val Pro Ile Pro Glu Glu Glu Lys
 210 215 220
 Lys Asp Glu Glu Lys Lys Asp Glu Glu Lys Lys Asp Glu Asp Asp Lys
 225 230 235 240
 Lys Pro Lys Leu Glu Glu Val Asp Glu Glu Glu Lys Lys Pro Lys
 245 250 255
 Thr Lys Lys Val Lys Glu Glu Val Gln Glu Ile Glu Glu Leu Asn Lys
 260 265 270
 Thr Lys Pro Leu Trp Thr Arg Asn Pro Ser Asp Ile Thr Gln Glu Glu
 275 280 285
 Tyr Asn Ala Phe Tyr Lys Ser Ile Ser Asn Asp Trp Glu Asp Pro Leu
 290 295 300
 Tyr Val Lys His Phe Ser Val Glu Gly Gln Leu Glu Phe Arg Ala Ile
 305 310 315 320
 Leu Phe Ile Pro Lys Arg Ala Pro Phe Asp Leu Phe Glu Ser Lys Lys
 325 330 335
 Lys Lys Asn Asn Ile Lys Leu Tyr Val Arg Arg Val Phe Ile Thr Asp
 340 345 350
 Glu Ala Glu Asp Leu Ile Pro Glu Trp Leu Ser Phe Val Lys Gly Val
 355 360 365
 Val Asp Ser Glu Asp Leu Pro Leu Asn Leu Ser Arg Glu Met Leu Gln
 370 375 380
 Gln Asn Lys Ile Met Lys Val Ile Arg Lys Asn Ile Val Lys Lys Leu
 385 390 395 400
 Ile Glu Ala Phe Asn Glu Ile Ala Glu Asp Ser Glu Gln Phe Glu Lys
 405 410 415
 Phe Tyr Ser Ala Phe Ser Lys Asn Ile Lys Leu Gly Val His Glu Asp
 420 425 430
 Thr Gln Asn Arg Ala Ala Leu Ala Lys Leu Leu Arg Tyr Asn Ser Thr
 435 440 445
 Lys Ser Val Asp Glu Leu Thr Ser Leu Thr Asp Tyr Val Thr Arg Met

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450	455	460
Pro Glu His Gln Lys Asn Ile Tyr Tyr Ile Thr Gly Glu Ser Leu Lys 465	470	475
Ala Val Glu Lys Ser Pro Phe Leu Asp Ala Leu Lys Ala Lys Asn Phe 485	490	495
Glu Val Leu Phe Leu Thr Asp Pro Ile Asp Glu Tyr Ala Phe Thr Gln 500	505	510
Leu Lys Glu Phe Glu Gly Lys Thr Leu Val Asp Ile Thr Lys Asp Phe 515	520	525
Glu Leu Glu Glu Thr Asp Glu Glu Lys Ala Glu Arg Glu Lys Glu Ile 530	535	540
Lys Glu Tyr Glu Pro Leu Thr Lys Ala Leu Lys Glu Ile Leu Gly Asp 545	550	555
Gln Val Glu Lys Val Val Val Ser Tyr Lys Leu Leu Asp Ala Pro Ala 565	570	575
Ala Ile Arg Thr Gly Gln Phe Gly Trp Ser Ala Asn Met Glu Arg Ile 580	585	590
Met Lys Ala Gln Ala Leu Arg Asp Ser Ser Met Ser Ser Tyr Met Ser 595	600	605
Ser Lys Lys Thr Phe Glu Ile Ser Pro Lys Ser Pro Ile Ile Lys Glu 610	615	620
Leu Lys Lys Arg Val Asp Glu Gly Gly Ala Gln Asp Lys Thr Val Lys 625	630	635
Asp Leu Thr Lys Leu Leu Tyr Glu Thr Ala Leu Leu Thr Ser Gly Phe 645	650	655
Ser Leu Asp Glu Pro Thr Ser Phe Ala Ser Arg Ile Asn Arg Leu Ile 660	665	670
Ser Leu Gly Leu Asn Ile Asp Glu Asp Glu Glu Thr Glu Thr Ala Pro 675	680	685
Glu Ala Ser Thr Ala Ala Pro Val Glu Glu Val Pro Ala Asp Thr Glu 690	695	700
Met Glu Glu Val Asp 705		

<210> 330

<211> 260

<212> PRT

<213> Rana esculenta

<400> 330

Glu Met Ala Ser Leu Ser Glu Tyr Val Ser Arg Met Lys Glu Thr Gln

299/299

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Lys Ser Ile Tyr Tyr Ile Thr Gly Glu Ser Lys Glu Gln Val Ala Asn	20	25	30
Ser Ala Phe Val Glu Arg Val Arg Lys Arg Gly Phe Glu Val Val Tyr	35	40	45
Met Thr Glu Pro Ile Asp Glu Tyr Cys Val Gln Gln Leu Lys Glu Phe	50	55	60
Asp Gly Lys Thr Leu Val Ser Val Thr Lys Glu Gly Leu Glu Leu Pro	65	70	75
Glu Asp Asp Glu Glu Lys Lys Lys Met Glu Glu Asn Lys Thr Lys Phe	85	90	95
Glu Gly Leu Cys Lys Leu Met Lys Glu Ile Leu Asp Lys Lys Val Glu	100	105	110
Lys Val Thr Val Ser Asn Arg Leu Val Ser Ser Pro Cys Cys Ile Val	115	120	125
Thr Ser Thr Tyr Gly Trp Thr Ala Asn Met Glu Arg Ile Met Lys Ala	130	135	140
Gln Ala Leu Arg Asp Asn Ser Thr Met Gly Tyr Met Met Ala Lys Lys	145	150	155
His Leu Glu Ile Asn Pro Glu His Pro Ile Val Glu Thr Leu Arg Gln	165	170	175
Lys Ala Glu Ala Asp Lys Asn Asp Lys Ala Val Lys Asp Leu Val Val	180	185	190
Leu Leu Phe Glu Thr Ala Leu Leu Ser Ser Gly Phe Ser Leu Asp Asp	195	200	205
Pro Gln Thr His Ser Asn Arg Ile Tyr Arg Met Ile Lys Leu Gly Leu	210	215	220
Gly Ile Asp Glu Asp Glu Pro Ala Ile Glu Glu Thr Thr Ala Ala Val	225	230	235
Pro Asp Asp Ile Pro Pro Leu Glu Gly Glu Glu Asp Ala Ser Arg Met	245	250	255
Glu Glu Val Asp	260		

DERWENT-ACC-NO: 2002-698710**DERWENT-WEEK:** 200817*COPYRIGHT 2010 DERWENT INFORMATION LTD*

TITLE: Treating genetically-defined disease associated with chromosomal aberrations yielding oncogenic fusion proteins, e.g. cell proliferative diseases, involves administering an inhibitor of heat shock protein 90

INVENTOR: BURROWS F; BURROWS F J ; FRITZ L ; FRITZ L
C

PATENT-ASSIGNEE: BURROWS F[BURRI] , CONFORMA
THERAPEUTIC CORP[CONFN] , CONFORMA
THERAPEUTICS CORP[CONFN] , FRITZ L
[FRITI]

PRIORITY-DATA: 2001US-272751P (March 1, 2001) ,
2002WO-US06518 (March 1, 2002) ,
2003US-469469 (August 27, 2003) ,
2007US-779243 (July 17, 2007)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE
WO 02069900 A2	September 12, 2002	EN
AU 2002252179 A1	September 19, 2002	EN
EP 1423080 A2	June 2, 2004	EN
US 20060079493 A1	April 13, 2006	EN
AU 2002252179 A8	October 27, 2005	EN
US 20080051462 A1	February 28, 2008	EN

DESIGNATED-STATES: AE AG AL AM AT AU AZ BA BB BG BR
 BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EC EE ES FI GB GD GE GH GM
 HR HU ID IL IN IS JP KE KG KP KR
 KZ LC LK LR LS LT LU LV MA MD MG
 MK MN MW MX MZ NO NZ OM PH PL PT
 RO RU SD SE S G SI SK SL TJ TM TN
 TR TT TZ UA UG US UZ VN YU ZA ZM
 ZW AT BE CH CY DE DK EA ES FI FR
 GB GH GM GR IE IT KE LS LU MC MW
 MZ NL OA PT SD SE SL SZ TR TZ UG
 ZM ZW AL AT BE CH CY DE DK ES FI
 FR GB GR IE IT LI LT LU LV MC MK
 NL PT RO SE SI TR

APPLICATION-DATA:

PUB-NO	APPL-DESCRIPTOR	APPL-NO	APPL-DATE
WO2002069900A2	N/A	2002WO- US06518	March 1, 2002
AU2002252179A1	N/A	2002AU- 252179	March 1, 2002
AU2002252179A8	N/A	2002AU- 252179	March 1, 2002
EP 1423080A2	N/A	2002EP- 721238	March 1, 2002
EP 1423080A2	N/A	2002WO- US06518	March 1, 2002
US20060079493A1	N/A	2002WO- US06518	March 1, 2002
US20060079493A1	N/A	2003US- 469469	August 27, 2003
US20080051462A1	Based on	2007US- 779243	July 17, 2007

INT-CL-CURRENT:

TYPE	IPC DATE
CIPP	A61K31/135 20060101
CIPP	A61K31/33 20060101
CIPS	A61K31/395 20060101
CIPS	A61P35/00 20060101
CIPS	A61P43/00 20060101
CIPS	C12P21/08 20060101
CIPS	C12Q1/68 20060101
CIPS	G01N33/53 20060101

ABSTRACTED-PUB-NO: WO 02069900 A2

BASIC-ABSTRACT:

NOVELTY - Treating (M) genetically-defined disease associated with chromosomal aberrations yielding oncogenic fusion proteins (I), treating cancerous cells containing (I) in a heterogeneous cell population, treating proliferative diseases (PD) associated with mutant protein or cellular protein isoforms (II) dependent on heat shock protein (HSP)-90, or selectively treating cells expressing (II), involves administering HSP90-inhibitor.

DESCRIPTION - A method (M) comprising:

(a) treating a patient having a genetically-defined disease characterized by a chromosomal aberration that yields an oncogenic fusion protein, by providing a cell, tissue or fluid sample of a patient suspected of having the genetically-defined disease, identifying one or more characteristics indicative of the disease

in or on the cell, tissue or fluid sample, and administering to the patient, a pharmaceutically effective amount of HSP90-inhibiting compound (III);

(b) treating cancerous cells in a heterogeneous population of cells (the heterogeneous population comprises both cancerous and non-cancerous cells and cancerous cells being characterized by fusion proteins not found in noncancerous cells), by administering a pharmaceutically effective amount of (III) to the heterogeneous population of cells;

(c) treating a patient having a proliferative disease associated with a mutant protein or cellular protein isoform (II) dependent on HSP90, by providing a cell, tissue, or fluid sample of a patient suspected of having the proliferative disease, identifying in the cell, tissue, or fluid sample one or more characteristics indicative of (II), and administering a pharmaceutically effective amount of (III) to the patient; or

(d) selectively treating cells that express (II) that gives to a proliferative disorder dependent on HSP90, by providing a population of cells in which at least some of the population express (II) that is differentially dependent on HSP90 for effect and gives rise to a proliferative disorder, and administering a pharmaceutically effective amount of (III) to the population.

HSP-90 inhibitor (claimed).

USE - (M) Is useful for treating genetically-defined disease with chromosomal aberration yielding oncogenic fusion protein, treating cancerous cells containing fusion protein in heterogeneous cell population, treating proliferative disease (e.g. rheumatoid arthritis or cancer) associated with mutant protein or

cellular protein isoform dependent on heat shock protein (HSP)-90 (e.g. p53), or selectively treating cells expressing mutant protein or cellular protein isoform in a patient heterozygous for (II).

(M) Is useful for treating a disease e.g. hematopoietic disorder such as T or B cell lymphoma, chronic myeloid leukemia (CML), APL, ALL, AML, NHL and CMML, or a disease characterized by a solid tumor such as papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma and synovial sarcoma (claimed).

(M) is also useful for treating viral infections.

EQUIVALENT-ABSTRACTS:

BIOTECHNOLOGY

Preferred Compound: (III) Is ansamycin e.g. geldanamycin, 17-AAG, herbimycin A and macbecin, or radicicol or its analog. (III) binds into the ATP-binding site of a HSP90.

Preferred Method: (M) Further involves identifying a nucleic acid encoding (I), by using polymerase chain reaction (PCR) or ligase chain reaction (LCR), using an antibody to identify (I), or using a cytochemical technique which employs nucleic acid hybridization (e.g. fluorescence in situ hybridization (FISH)). (I) contains one or more functional domains or their portions of kinases and DNA binding motifs. The method is an ex vivo method.

(III) Has an IC(50) at least 2-10 fold higher for cells that do not have characteristics indicative of the genetically-defined proliferative disorder relative to those cells that do have such characteristics. The cells of the patient are

monitored in vitro for sensitivity prior to administration of (III) to the patient. The non-random chromosomal aberration is translocation, inversion or deletion. The non-random chromosomal aberration is selected from any one of the aberrations given in the specification, e.g. t(9;22)(q34;q11) optionally characterized by and comprising a sequence of 63, 63, 423, 222, 1079 or 106 nucleotides fully defined in the specification (encoding a sequence of 21, 21, 140, 307, 359 or 34 amino acids fully defined in the specification), or its homolog, isoform or allelic variant.

Alternately, (III) has an IC(50) that is at least 5-10 fold lower for the cancerous cells than for the noncancerous cells within heterogeneous population, and where the pharmaceutically effective amount administered is about half or less of the IC(50) of the noncancerous cells. Treatment is monitored by PCR, antibody staining or nucleic acid hybridization, which are selective for the presence of cancerous cells.

(I) Has a heightened dependence on HSP90.

(III) Is a synthetic analog of geldanamycin.

(II) is src, RET, p53, p51, p63, p73, or their homologs and allelic variations. (II) is a dominant negative mutant, e.g. human p53 such as N239S, C176R, and R213asterisk, Y236DELTA, C176Y, M133T, G245D, E258K, 1-293 DELTA, G245C, R248W, E258K, R282W, R175HU, R280K, V143A, R175H, P177S, H178P, H179R, R181P, 138-9DELTA, G245S, G245D, M246R, R248Q, R249S, R273H, R273C, R273L, and D218Y.

Alternately, (II) is a dominant positive mutant or a C176Y mutant.

(III) Is administered through intralesional or

parenteral route (claimed).

(III) is administered at a dose of 0.01-100 mg/kg body weight, preferably 0.1-10 mg/kg body weight.

TITLE-TERMS: TREAT GENETIC DEFINE DISEASE ASSOCIATE
CHROMOSOME ABERRATION YIELD ONCOGENIC
FUSE PROTEIN CELL PROLIFERATION
ADMINISTER INHIBIT HEAT SHOCK

DERWENT-CLASS: B04 B05 D16

CPI-CODES: B04-B04C2; B04-C01G; B04-E03F; B04-E05;
B04-G01; B04-N02A0E; B11-A02; B11-C07A;
B11-C08E; B11-C08F; B11-C08G; B12-K04A1;
B14-C06; B14-C09; B14-H01; B14-S03; D05-A02B;
D05-H07; D05-H08; D05-H09; D05-H11; D05-H12A;
D05-H12D1; D05-H18; D05-H18B;

CHEMICAL-CODES: Chemical Indexing M1 *06*
Fragmentation Code M423 M750 N102
N134 N152 Q233 Specific Compounds
RA00NS Registry Numbers 93605

Chemical Indexing M1 *07*
Fragmentation Code M423 M750 N102
N134 N152 Q233 Specific Compounds
RA012P Registry Numbers 105730

Chemical Indexing M1 *08*
Fragmentation Code M417 M423 M430
M782 N102 N134 N152 P831 Q233 Q505
Specific Compounds RA013I Registry
Numbers 184610

Chemical Indexing M1 *09*
Fragmentation Code M423 M430 M782
N102 N134 N152 P831 Q233 Q505
Specific Compounds RA031J Registry

Numbers 204310 204644

Chemical Indexing M1 *10*
Fragmentation Code M417 M423 M781
N102 P831 Q233 Q505 Specific
Compounds RA00C8 Registry Numbers
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Chemical Indexing M1 *11*
Fragmentation Code M417 M423 M750
N102 Q233 Specific Compounds RA00H1
Registry Numbers 184611

Chemical Indexing M1 *12*
Fragmentation Code M417 M423 M750
N102 Q233 Specific Compounds RA00H3
Registry Numbers 184616

Chemical Indexing M1 *13*
Fragmentation Code M417 M423 M750
N102 N136 Q233 Specific Compounds
RA00GT Registry Numbers 200757 200799

Chemical Indexing M2 *01*
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H521 H8 J0 J011 J2 J221 J5 J522 J561
K0 L9 L941 L951 M210 M211 M214 M232
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P423 P631 P633 Q233 Ring Index
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Compounds R18825 Registry Numbers
105651

Chemical Indexing M2 *02*
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M520 M530 M540 M781 P421 P423 P631
P633 Q233 Ring Index Numbers 47148
Specific Compounds RA0V2E Registry
Numbers 95974

Chemical Indexing M2 *03*
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Registry Numbers 162868

Chemical Indexing M2 *04*
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M320 M412 M511 M520 M530 M540 M781
P421 P423 P631 P633 Q233 Ring Index
Numbers 47148 Specific Compounds
RA2RSN Registry Numbers 334393

Chemical Indexing M2 *05*
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51839 Specific Compounds R04889
Registry Numbers 101246

Chemical Indexing M6 *14*
Fragmentation Code P421 P423 P631
P633 P831 Q233 Q505 R231 R502 R515

R520 R521 R614 R621 R624 R627 R631
R637 R639

SECONDARY-ACC-NO:

CPI Secondary Accession Numbers: 2002-197903